STRUCTURE-REACTIVITY RELATIONSHIPS OF LITHIUM AMIDES: LIHMDS-MEDIATED ENOLIZATIONS OF HINDERED ARYL KETONES AND LITMP-MEDIATED ORTHOLITHIATIONS

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Doctor of Philosophy

by

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Kyle Anthony Mack, Ph. D.

Cornell University 2018

Enolizations of highly substituted acyclic ketones used in the syntheses of tetrasubstituted olefin-based anticancer agents are described. Lithium hexamethyldisilazide (LiHMDS)-mediated enolizations are moderately *Z*-selective in neat tetrahydrofuran (THF) and *E*-selective in 2.0 M THF/hexane. The results of NMR spectroscopy show the resulting enolates to be statistically distributed ensembles of *E*,*E*-, *E*,*Z*-, and *Z*,*Z*-enolate dimers with subunits that reflect the selectivities. The results of rate studies trace the preference for *E* and *Z* isomers to tetrasolvated- and pentasolvated-monomer-based transition structures, respectively. Enolization using LiHMDS in *N*,*N*-dimethylethylamine or triethylamine in toluene affords a 65:1 mixture of LiHMDS−lithium enolate mixed dimers containing *E* and *Z* isomers, respectively. Spectroscopic studies show that condition-dependent complexation of ketone to LiHMDS occurs in trialkylamine/toluene. Rate data attribute the high selectivity exclusively to monosolvated-dimer-based transition structures.

Rate and mechanistic studies of ortholithiations by lithium 2,2,6,6-tetramethylpiperidine focus on four arenes: 1,4-bis(trifluoromethyl)benzene, 1,3-bis(trifluoromethyl)benzene, 1,3-dimethoxybenzene, and 4,4-dimethyl-2-phenyl-2-oxazoline. Metalations occur via substrate-dependent combinations of monosolvated monomer, disolvated monomer, and tetrasolvated dimer (triple ions). Density functional theory computational studies augment the experimental data. We discuss the challenges presented by shifting dimer–monomer proportions in

determining the observable reaction orders and our mathematical treatment of such shifting in reactant structure.

BIOGRAPHICAL SKETCH

The author was born on June 23, 1991 in New Brunswick, NJ to Mr. Joseph A. Mack and Mrs. Jennifer E. Mack. After completing his secondary education at Delaware Valley Regional High School in Frenchtown, NJ he attended Raritan Valley Community College and attained an A.S. with a focus in Pre-Medical science. He then transferred to Montclair State University. Under the guidance of Prof. Hans Schelvis he studied the mechanism of repair for UV-irradiated DNA by the photolyase enzyme. The author received his B.S. in Chemistry with a minor in Mathematics and graduated *summa cum laude* in 2013. In addition, he was awarded the Margaret and Herman Sokol Graduate Fellowship in Science. Later that year, he began his graduate studies at Cornell University in the laboratory of Prof. David B. Collum. His graduate work focused on how mechanistic studies of organolithium-mediated transformations could augment synthetic methods. The author received an M.S. in May 2015 and a Ph. D. in May 2018.

This work is dedicated to my brother,

Ryan J. Mack

For the endless pursuit of happiness

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I will begin by acknowledging the opportunity that was given to me by Prof. David B. Collum to perform graduate research in his laboratory. He support academically was invaluable, while his eccentric personality could make even the dullest of days more palatable. Prof. Collum, as a friend and mentor, is truly worth his weight in gold. I would also like to express gratitude to those currently serving on my special committee, Prof. Geoffrey W. Coates and Prof. Brett P. Fors, as well as past member Prof. William R. Dichtel.

The members of the Collum group during my time at Cornell University provided training and an intellectually stimulating work environment. I had the pleasure of working alongside research associate Dr. Yun Ma, postdoctoral associate Dr. Gabriel J. Reyes-Rodríguez, and fellow graduate students Dr. Laura L. Tomasevich, Dr. Jun Liang, Dr. Kyong Joo Jin, Dr. Michael Houghton, Ms. Jacqueline Perodeau, Dr. Russell F. Algera, Dr. Janis Jermaks, Ms. Yuhui Zhou, Ms. Zirong Zhang, Mr. Jackson Clark, and Mr. Ryan Woltornist. They have all, in some meaningful way, contributed to this work. I would also like to recognize the undergraduate researchers who have spent time in the lab, especially Taylor Jordan who I mentored.

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Finally, I would like to acknowledge those who I call family. My parents, Mr. Joseph A. Mack and Mrs. Jennifer E. Mack have encouraged my pursuit of education and supported all of my decisions along the way. My brothers, Mr. Ryan J. Mack and Mr. Brendan R. Mack, have constantly reminded me to enjoy life. Mr. Michael Cedro, Mrs. Yong Cedro, Morgan Evans, and

Sarah Cedro have shown me that the love and support of a family can extend beyond blood. Lastly, my grandfather, Robert P. Price, taught me that curiosity and ingenuity are every bit as important to success as raw knowledge.

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CHAPTER 1

LITHIUM HEXAMETHYLDISILAZIDE-MEDIATED ENOLIZATIONS OF HIGHLY SUBSTITUED ARYL KETONES: STRUCTURAL AND MECHANISITIC BASIS OF THE *E*/*Z* SELECTIVITIES

Lithium Hexamethyldisilazide Mediated Enolizations of Highly Substituted Aryl Ketones: Structural and Mechanistic Basis of the *E/Z* Selectivities

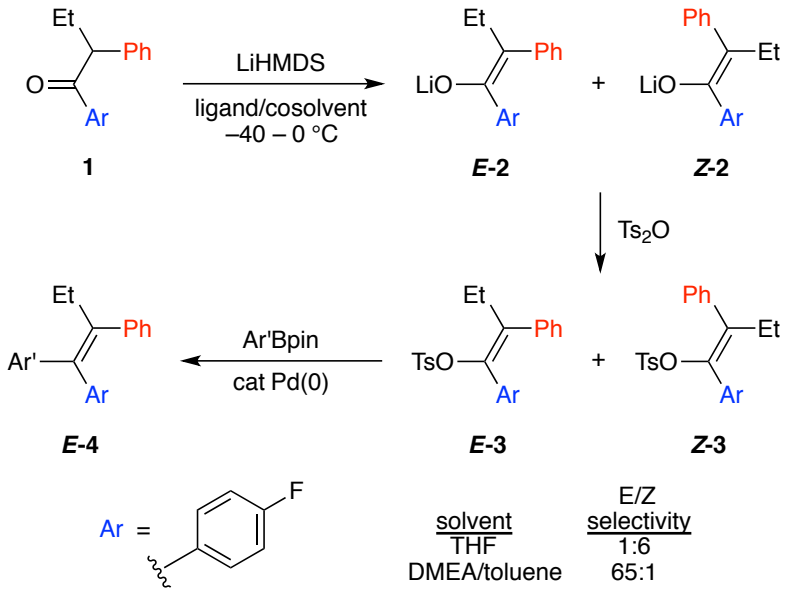
Abstract

Enolizations of highly substituted acyclic ketones used in the syntheses of tetrasubstituted olefin-based anticancer agents are described. Lithium hexamethyldisilazide (LiHMDS)-mediated enolizations are moderately *Z*-selective in neat tetrahydrofuran (THF) *E*-selective in 2.0 M THF/hexane. NMR spectroscopy shows the resulting enolates to be statistically distributed ensembles of *E*,*E*-, *E*,*Z*-, and *Z*,*Z*-enolate dimers with subunits that reflect the selectivities. The results of rate studies trace the preference for *E* and *Z* isomers to tetrasolvated- and pentasolvated-monomer-based transition structures, respectively. Enolization using LiHMDS in *N*,*N*-dimethylethylamine or triethylamine in toluene affords a 65:1 mixture of LiHMDS–lithium enolate mixed dimers containing *E* and *Z* isomers, respectively. Spectroscopic studies show that condition-dependent complexation of ketone to LiHMDS occurs in trialkylamine/toluene. Rate study findings attribute the high selectivity exclusively to monosolvated-dimer-based transition structures.

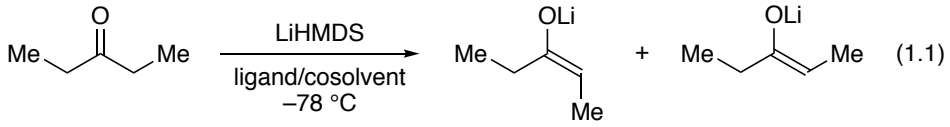
Introduction

As part of our program to develop GDC-0810, a selective estrogen receptor degrader currently in clinical trials for the treatment of breast cancer,[1] we required an efficient and stereoselective synthesis of a tetrasubstituted acyclic all-carbon olefin, a structural motif central to a number of anticancer agents including tamoxifen,[2] idoxifene,[3] and etacstil.[4] Our strategy, outlined in Scheme 1.1, was fraught with challenges, not the least of which was the requisite *E*-selective enolization en route to desired olefin ***E*-4**.[5]

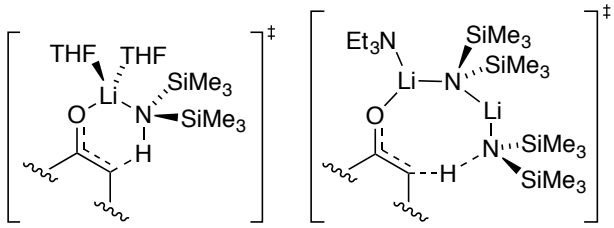
Scheme 1.1. Strategy for the stereoselective synthesis of tetrasubstituted acyclic all-carbon olefins.



The plan was founded on lithium hexamethyldisilazide (LiHMDS)-mediated enolizations of much simpler ketones showing highly solvent-dependent *E/Z* selectivities (eq 1.1).[6] The dependencies in such uncongested cases derive from markedly different mechanisms corresponding to monomer- and dimer-based transition structures **5** and **6**,[7,8] which offered the possibility that the stereoselectivity would extend to the stereochemically demanding case in Scheme 1.1. Indeed, 65:1 *E/Z* selectivity exceeded expectations.[5] In this paper, we describe the combination of spectroscopic, kinetic, and computational methods used to ascertain the origins of the low selectivities observed with LiHMDS/tetrahydrofuran (THF) and the high selectivities observed with LiHMDS/trialkylamine/toluene.



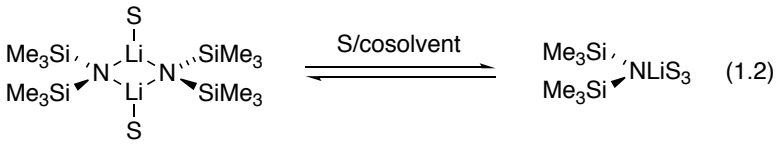
solvent	E/Z selectivity
THF	1:4
Et_3N/toluene	140:1



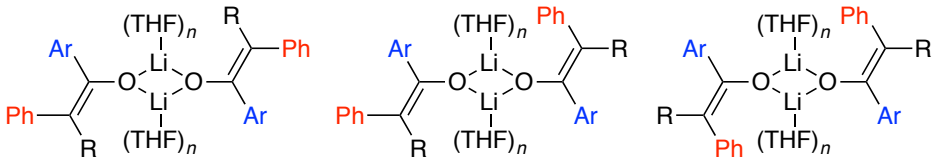
5 **6**

Results

General. LiHMDS, [^{6}Li]LiHMDS, and [^{6}Li,^{15}N]LiHMDS were prepared and purified as white crystalline solids.[9] Previous studies of LiHMDS described solvent-dependent dimer-monomer mixtures (eq 1.2), although the equilibrium was surprisingly sensitive to the choice of hydrocarbon cosolvent (*vide infra*).[10,11] Rate studies were undertaken using the tactics described in two reviews.[12] Density functional theory (DFT) computations were carried out at the B3LYP/6-31G(d) level of theory[13] with single-point MP2 calculations.



7 **8**



***E,E*-2** ***E,Z*-2** ***Z,Z*-2**

Enolate Structures: THF. The enolization of **1** using [^{6}Li,^{15}N]LiHMDS in neat THF at 0 °C afforded an ensemble of three resonances recorded at –80 °C and designated ***E,E*-2**, ***E,Z*-2**, and ***Z,Z*-2** (1:32:67; Figure 1.1A). This result was consistent with the approximate 1:6 *E/Z* selectivity shown with tosylation and subsequent high-performance liquid chromatography analysis.[5] The absence of resonances displaying ^{6}Li–^{15}N coupling confirmed that detectable mixed aggregates were not present. As the THF concentration decreased, the distribution of enolates shifted to favor ***E*-2** (Figure 1.1B–D) with a concurrent shift in the distribution of isomeric trapped tosylates. The method of continuous variation,[14] was used to plot of the relative populations of ***E,E*-2**, ***E,Z*-2**, and ***Z,Z*-2** versus measured mole fraction[15] of the ***E*-2** subunit (χ_E) and obtain a Job plot[16] (Figure 1.2) confirming the dimer assignment.

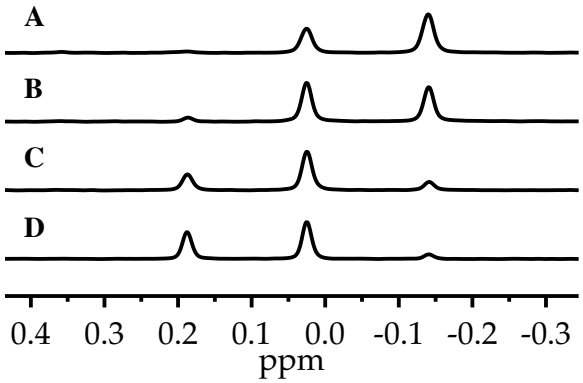


Figure 1.1. ^{6}Li NMR spectra of mixtures containing ***E,E*-2**, ***E,Z*-2**, and ***Z,Z*-2** from 0.10 M [^{6}Li,^{15}N] LiHMDS (showing no coupling) and 0.10 M **1** in THF/hexane at –80 °C after aging at 0 °C for 48 h: (A) neat THF (12.2 M); (B) 6.0 M THF/hexane; (C) 4.5 M THF/hexane; and (D) 3.0 M THF/hexane. The measured mole fractions (χ_E) of ***E*-2** in A–D are 0.17, 0.30, 0.56, and 0.66, respectively.

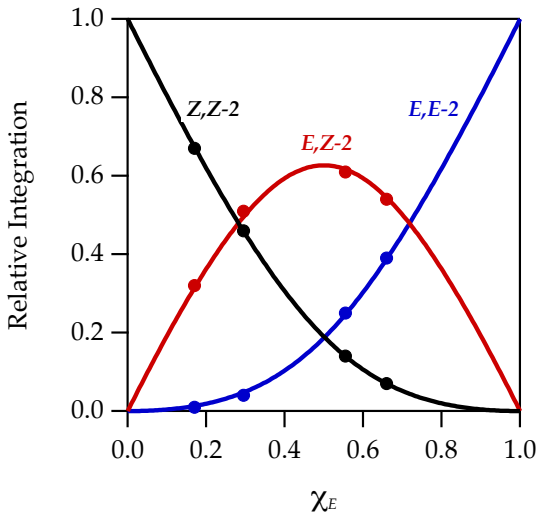


Figure 1.2. Job plot showing the relative integration of the ^{6}Li resonances versus the measured mole fraction (X_E)[15] of ***E*-2** for 0.10 M mixtures of ***E*- 2** and ***Z*-2** at –80 °C at varying THF concentrations in hexane (see Figure 1.1).

At <3.0 M THF (the right side of Figure 1.2), enolate insolubility became a problem. On a positive note, we obtained an X-ray crystal structure that, although of marginal quality, showed a trisolvated tetramer (Figure 1.3).

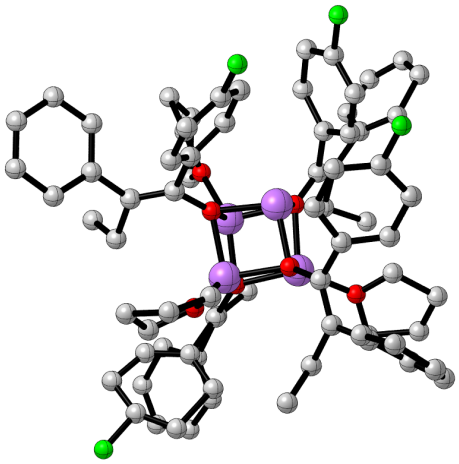


Figure 1.3. Low-resolution X-ray crystal structure of **2** crystallized from 0.10 M enolate generated in 2.0 M THF/hexane solutions. The compound is a trisolvated tetramer composed of four ***E*-2** subunits.[17]

Computational studies at the B3LYP level of theory with the 6-31G(d) basis set and MP2 correction[13,14] were used to probe some of the inherent properties of the enolate dimers. Serial solvation showed that ***E,E*-2**, ***E,Z*-2**, and ***Z,Z*-2** saturated at tetrasolvation (n = 2). The heterodimer ***E,Z*-2** showed a small (0.4 kcal/mol) net stabilization, as observed experimentally.

Mechanism of Enolization: THF. Enolizations of **1** (0.010 M) with LiHMDS (0.020–0.20 M) in THF/hexane mixtures (2.0–12.2 M THF) were followed at 0 °C. The results of in situ IR spectroscopy[18] showed that the loss of **1** (1687 cm^{-1}) followed a first-order decay. The pseudo-first-order rate constants (k_{obsd}) were independent of the initial concentration of **1**, consistent with a first-order ketone dependence. Ketone **1** deuterated at the 2-position (**1-*d*$_1$**) afforded an isotope effect (k_H/k_D = 6) consistent with rate-limiting proton transfer.

A plot of initial rates[19] versus THF concentration revealed a deceptively simple dependence; a fit to rate = a[THF]^n afforded n = 2.8 (Figure 1.4, inset). The deception stemmed from the shift of >95% disolvated dimer in 2.0 M THF/hexane to >95% trisolvated monomer in neat THF (eq 1.2).[10] A simple power function did not account for the dimer-monomer equilibrium or the affiliated change in solvation per Li. If the reaction had proceeded via a single mechanism involving disolvated monomer (AS_2), such as transition structure **5**, a maximum in the plot at intermediate THF concentrations would have been observed.[20] That the rates continue rising even as trisolvated monomer becomes dominant demands that an even more highly solvated form be involved in the enolization. By monitoring the THF-dependent *E/Z* selectivities over the analogous range of THF concentrations, we separated the components of the two pathways and showed that they contribute to second- and third-order dependencies (see Figure 1.4, curves A and B, respectively). Once again, these orders, which are consistent with the measured ratios, were *not* trivial to extract from the data and required fitting to the model discussed below and described in the supporting information. Using toluene in place of hexane resulted in no measurable difference in the THF dependence, which seems self-evident except that pronounced hydrocarbon effects on LiHMDS/THF-mediated enolizations have been observed.[20]

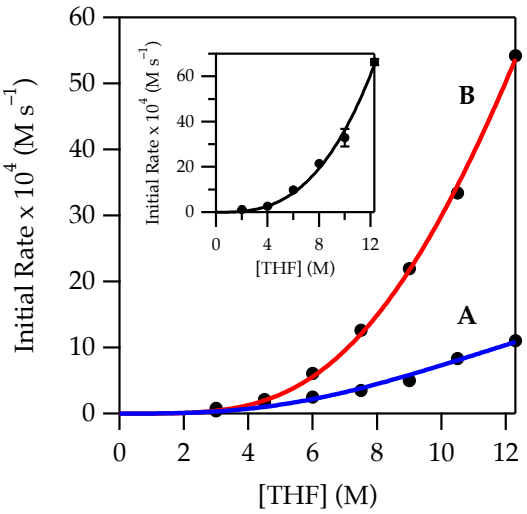


Figure 1.4. Plot of initial rate vs THF concentration in hexane for the enolization of **1** (0.010 M) with LiHMDS (0.10 M) at 0 °C measured with IR spectroscopy (1687 cm^{-1}). The inset depicts an unweighted least-squares fit to $y = ax^n$ [$a = 0.05 \pm 0.03$, $n = 2.8 \pm 0.2$]. Curves A and B represent unweighted least-squares fits to each half of eq 1.3 (k_1 and k_2, respectively) with $A_2(THF)_2$ described in eq 1.4. The initial rates for the formation of ***E*-2** were determined by multiplying the proportion of ***E*-2** at a given THF concentration by the total initial rate at that concentration. The initial rates of ***Z*-2** formation were calculated similarly.

A plot of initial rates versus LiHMDS concentration in neat THF, conditions in which trisolvated monomer **8** (eq 1.2, S = THF) dominated (97%), showed a first-order dependence (Figure 1.5), confirming that the observable monomer reacts as a monomer. The analogous plot in 2.0 M THF/hexane, which favored dimer (96%), revealed an approximate half-order dependence (Figure 1.6) consistent with a dimer–monomer pre-equilibrium followed by a monomer-based metalation.

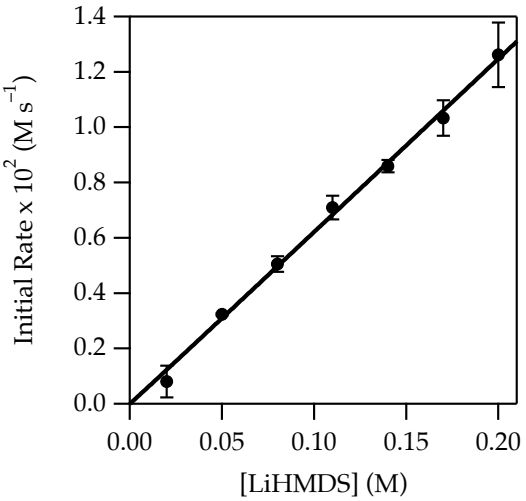


Figure 1.5. Plot of initial rate vs LiHMDS concentration in neat THF (12.2 M) for the enolization of **1** (0.010 M) at 0 ºC measured with IR spectroscopy (1687 cm^{-1}). The curve depicts an unweighted least-squares fit to $y = ax^n$ [$a = 6.3 \pm 0.5$, $n = 1.01 \pm 0.04$].

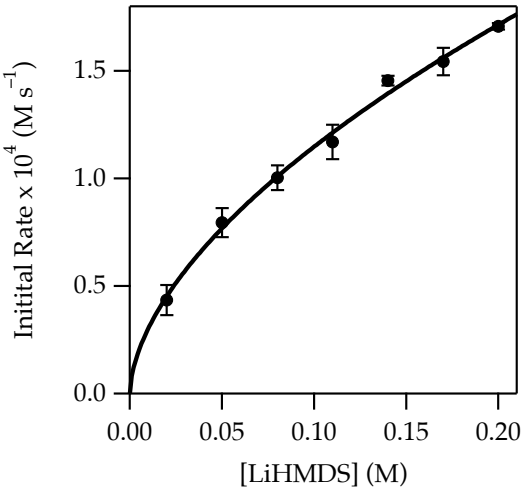


Figure 1.6. Plot of initial rate vs LiHMDS concentration in 2.0 M THF/hexane for the enolization of **1** (0.010 M) at 0 ºC measured with IR spectroscopy (1687 cm^{-1}). The curve depicts an unweighted least-squares fit to $y = ax^n$ [$a = 4.4 \pm 0.2$, $n = 0.58 \pm 0.02$].

The rate data are consistent with the rate law in eq 1.3 and the mechanism illustrated in eqs 1.4–1.7.[21] The complexity stems from solving for $[A_2(THF)_2]$ while accounting for both the shifting ground state—dimer to monomer—and the corresponding change in solvation number per Li. The underlying math is beyond the scope of this paper and is relegated to the supporting information.

$$\text{Rate} = (k_1[\text{THF}]^3 + k_2[\text{THF}]^4)[\mathbf{1}][A_2(THF)_2]^{1/2} \quad (1.3)$$

$$\left[A_2(\text{THF})_2\right] = \frac{1}{8}\left(4\left[A\right]_0 + K_{eq}\left[\text{THF}\right]^4 - \sqrt{K_{eq}}\left[\text{THF}\right]^2\sqrt{8\left[A\right]_0 + K_{eq}\left[\text{THF}\right]^4}\right) \quad (1.4)$$

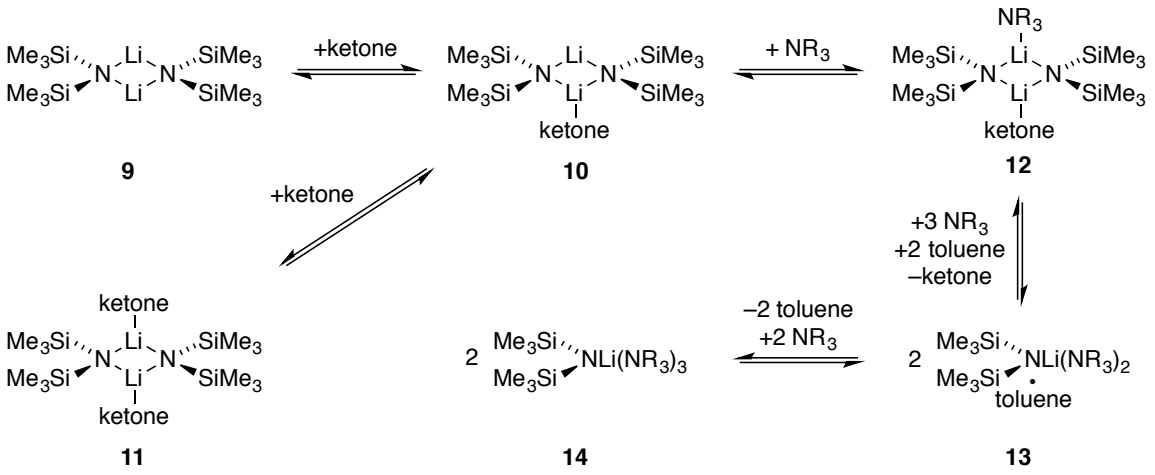
$$1/2\ A_2(THF)_2 + 2\ \text{THF} \overset{K_{eq}}{\rightleftharpoons} A(THF)_3 \quad (1.5)$$

$$A(THF)_3 + \mathbf{1} \xrightarrow{k_1[\text{THF}]} \text{E enolate} \quad (1.6)$$

$$A(THF)_3 + \mathbf{1} \xrightarrow{k_2[\text{THF}]^2} \text{Z enolate} \quad (1.7)$$

Structures of LiHMDS/ketone complexes: Trialkylamines. The rate studies of LiHMDS/trialkylamine-mediated enolizations were necessarily founded on the structural assignments of LiHMDS in the various trialkylamines with ketone present (Scheme 1.2). In weakly coordinating trialkylamines, LiHMDS–ketone complexes were readily observed. They differed quantitatively from analogous complexes formed from 2-methylcyclohexanone or 3-pentanone owing to weaker binding.[8]

Scheme 1.2. Condition-dependent equilibria for LiHMDS/ketone in DMEA with toluene hydrocarbon cosolvent.



In the absence of trialkylamines at –100 °C, ketone **1** complexed to LiHMDS dimer **9** to afford mono- and dicomplexed dimers **10** and **11**. Complex **10** displayed an IR absorbance at 1671 cm^{-1} and, in the NMR spectra, two ^{6}Li triplets (1:1) coupled to a single ^{15}N quintet. Complex **11** appeared as a ^{6}Li triplet and ^{15}N quintet. Complexation in the presence of trialkylamines depended on the structure of the amine. Triethylamine failed to convert **10** to **12** even at 5.0 M triethylamine (Et_3N). The less sterically demanding *N*,*N*-dimethylethylamine (DMEA), by contrast, readily afforded amine solvate **12** at >0.30 M DMEA. Elevated concentrations of DMEA converted **12** to LiHMDS monomer **14** and free ketone **1**, as shown with IR and NMR spectroscopies. Of importance to the rate studies was that complex **12** persisted as the dominant form of the ketone at elevated LiHMDS concentrations. Notably, ketone **1** was more easily dissociated than less hindered ketones.[8]

On first inspection, the inclusion of toluene-solvated monomer **13** may seem unusual. However, previous studies of LiHMDS/trialkylamines showed substantial hydrocarbon cosolvent effects.[11] Resolution precluded such investigations of DMEA/hydrocarbon mixtures. The results from spectroscopic studies using Et_2NMe/toluene mixtures illustrate qualitatively the magnitude

of such toluene effects on the dimer-monomer equilibria (Figure 1.7).

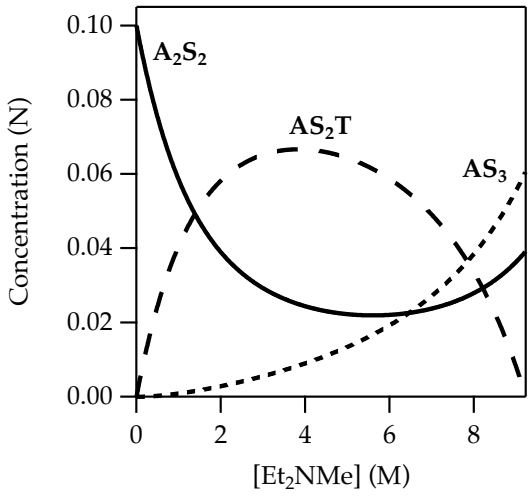
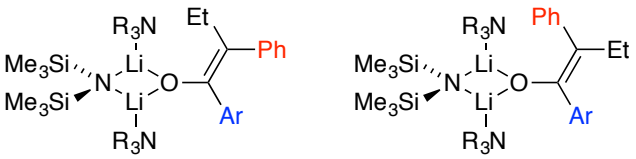


Figure 1.7. Simulated plot of LiHMDS aggregate concentrations— A_2S_2-AS_2T-AS_3—as a function of Et_2NMe concentration in toluene highlighting the influence of toluene.[11]

Enolate Structures: DMEA. Enolization of **1** using 1.0 equiv of LiHMDS in DMEA/toluene afforded homoaggregated enolates as broad mounds, which suggested oligomerization (possibly laddering[22]). By contrast, enolization using ≥2.0 equiv of [^{6}Li,^{15}N]LiHMDS afforded lithium enolate–LiHMDS mixed aggregate[8] ***E*-15** along with traces of ***Z*-15**, consistent with the 65:1 *E/Z* selectivity observed with tosylation.[6] The dimeric mixed aggregates displayed characteristic ^{6}Li–^{15}N coupling (3.6 Hz) and offered an independent measure of the *E*/*Z* selectivity. Treating the mixed dimers with THF afforded ***E,E*-2**, traces of ***E,Z*-2**, and free LiHMDS monomer. DFT computations were used to probe the solvation of LiHMDS–enolate mixed aggregates, and the *E*- and *Z*-enolate mixed dimers were shown to be disolvated ***E*-15** and ***Z*-15**, respectively.



***E*-15** ***Z*-15**

Enolization Mechanism: Et_3N. LiHMDS/Et_3N-mediated enolizations are mechanistically simple and familiar from previous studies.[8] The results of in situ IR spectroscopy showed that enolizations of **1** with LiHMDS in Et_3N/toluene at 0 °C involved first-order decays of complex **10** (1671 cm^{-1}). A kinetic isotope effect (k_H/k_D = 7) confirmed rate-limiting proton transfer. A plot of k_{obsd} versus Et_3N concentration (Figure 1.8) and *free* LiHMDS concentration (Figure 1.9) showed first and zeroth orders, respectively. Unsolvated complex **10** was observed spectroscopically. The rate law in eq 1.9 is consistent with the mechanism described by eqs 1.10 and 1.11. Replacing toluene with hexane caused a limited (1.3-fold) rate increase.

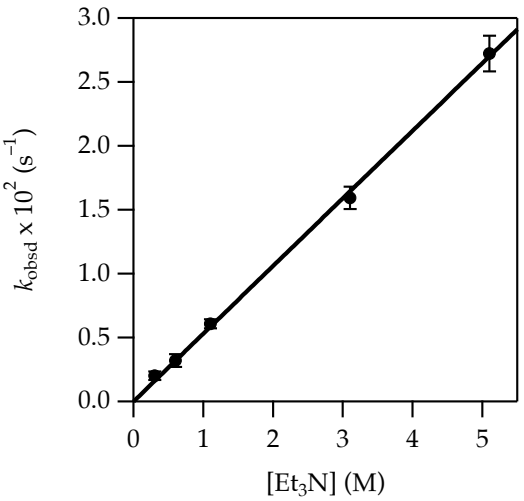


Figure 1.8. Plot of k_{obsd} vs Et_3N concentration in toluene for the enolization of **1** (0.0050 M) with LiHMDS (0.10 M) at 0 °C measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to $y = ax^n$ [a = 0.53 ± 0.03, n = 1.00 ± 0.03]. Analogous linearity and reaction order are replicated by the more complex function described in the text.

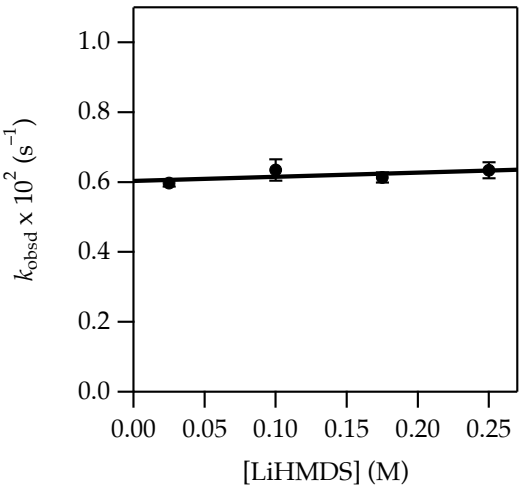


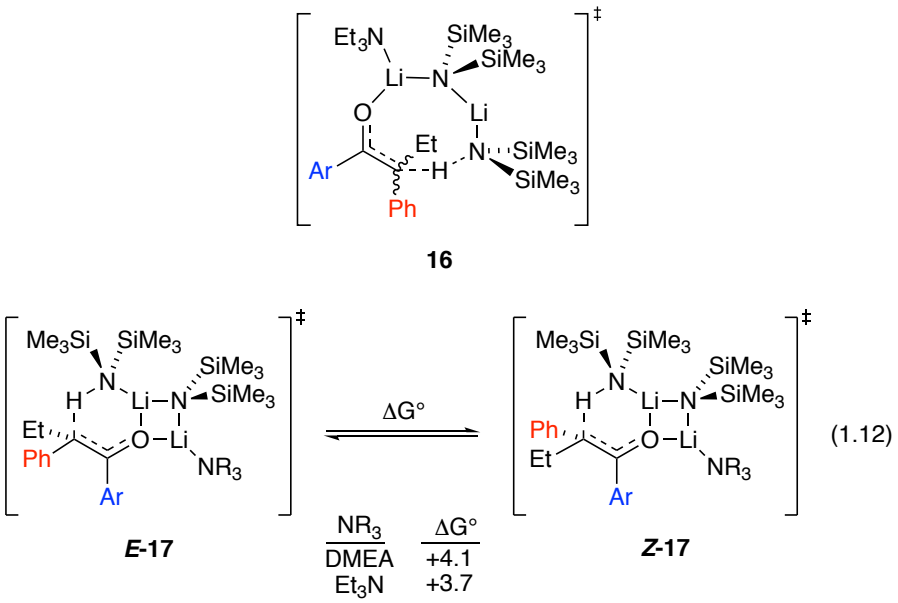
Figure 1.9. Plot of k_{obsd} vs LiHMDS concentration in 1.10 M Et_3N/toluene for the enolization of **1** (0.0025 M) at 0 ºC measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to y = ax + b [a = 0.60 ± 0.02, b = 0.1 ± 0.1].

$$d[\mathbf{10}]/dt = k[\mathbf{10}][Et_3N] \qquad (1.9)$$

$$A_2(\text{ketone}) \;(\mathbf{10}) \overset{K_{eq}[Et_3N]}{\rightleftharpoons} A_2(\text{ketone})(Et_3N) \;(\mathbf{12}) \qquad (1.10)$$

$$A_2(\text{ketone})(Et_3N) \;(\mathbf{12}) \xrightarrow{k} [A_2(Et_3N)(\text{ketone})]^{\ddagger} \;(\mathbf{17}) \qquad (1.11)$$

DFT computations of the dimer-based metalation were an attempt to probe open dimer-based transition structures (**16**) bearing 8-membered rings that allowed for optimal collinear proton transfer. In all cases, however, the computations converged on closed structures ***E*-17** and ***Z*-17** (eq 1.12). The relative energies were congruent with those of a highly *E*-selective enolization.



Enolization Mechanism: DMEA. Rate studies using DMEA were significantly more challenging owing to condition-dependent solution structures, as shown in Scheme 1.2. The enolizations of **1** with LiHMDS in 0.60 M DMEA/toluene at –40 °C—conditions favoring solvated complex **12**—showed first-order decays of **12** (1671 cm^{-1}), and the measured isotope effect (k_H/k_D = 8) confirmed rate-limiting proton transfer. Plotting k_{obsd} versus DMEA concentration (Figure 1.10) was complex, but the results were consistent with the observed structural changes: a first-order dependence at the low-DMEA-concentration limit akin to that observed for Et_3N abruptly gave way to inhibition owing to facile decomplexation (*vide infra*). Swapping toluene with hexane as the cosolvent (see Figure 1.10, inset) revealed an analogous result but with the maximum shifted to higher DMEA concentrations consistent with the relative stabilization of uncomplexed LiHMDS monomer with toluene versus hexane.

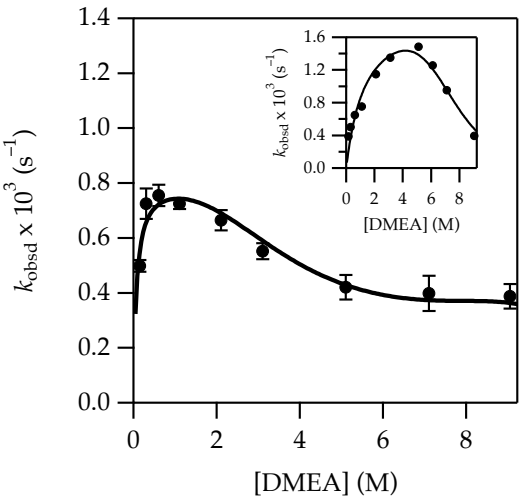


Figure 1.10. Plot of k_{obsd} vs DMEA concentration with toluene cosolvent for the enolization of **1** (0.0050 M) with LiHMDS (0.10 M) at –40 °C measured with IR spectroscopy (1687 cm^{-1}). The inset shows analogous data for hexane cosolvent. The curves depict unweighted least-squares fits to eq 1.13, which is described fully in the supporting information. Notably, the function describing the dependence of complex **12** in eq 1.13 changes with the choice of cosolvent.

A plot of k_{obsd} versus LiHMDS concentration (Figure 1.11) at 0.60 M DMEA revealed a zeroth-order dependence consistent with the direct reaction of complex **12**. Thus, the rate law at low DMEA concentration was consistent with that of a monosolvated-dimer-based enolization as observed for Et_3N (eq 1.9). A plot of k_{obsd} versus LiHMDS concentration in neat DMEA, conditions in which uncomplexed ketone dominated at low LiHMDS concentration and became complexed as dimer **12** at high LiHMDS concentration, showed second-order saturation (Figure 1.12). This result, in conjunction with the high *E/Z* selectivities determined with NMR spectroscopy and high-performance liquid chromatography analysis under these conditions, confirmed that monomer **14** *reaggregated* to complex **12** before reacting. The rate law and mechanism are described by eqs 1.13–1.15 below.

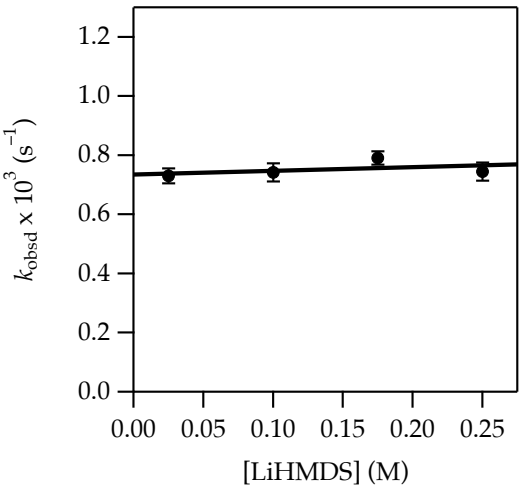


Figure 1.11. Plot of k_{obsd} vs LiHMDS concentration in 0.60 M DMEA/toluene for the enolization of **1** (0.0025 M) at –40 ºC measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to y = ax + b [a = 0.74 ± 0.02, b = 0.12 ± 0.02].

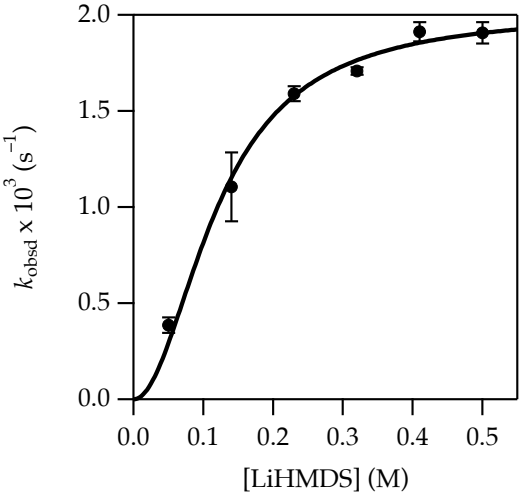


Figure 1.12. Plot of k_{obsd} vs LiHMDS concentration in neat DMEA (9.2 M) for the enolization of **1** (0.0050 M) at –40 °C measured with IR spectroscopy (1687 cm^{-1}). The curve depicts an unweighted least-squares fit to eq 1.13, which is described fully in the supporting information.

Mathematical Model. The rate of enolization is described by eq 1.13. The challenges of solving for the concentration of **12** were acute because this value is a function of the concentrations of four components (eq 1.14). The overall equation that describes the concentration of **12** is cumbersome (huge) and relegated to the supporting information. In brief, the model accounts for the complex curvatures shown in Figure 1.10. The flattening at high DMEA concentrations is not only demanded by the rate data but also by the known toluene dependence illustrated in Figure 1.7. The *second*-order saturation behavior in Figure 1.12 is also not unassailable from inspection but is required by the observable LiHMDS-concentration-dependent reaggregation of monomer **14** to form complexed LiHMDS dimer **12** at the saturation plateau. Finally, the model includes provisions for the simple dependencies in Figures 1.8, 1.9, and 1.11, which call for much simpler functions in the absence of knowledge of the shifting structures.

$$\mathrm{d}[\mathbf{15}]/\mathrm{d}t = k'[\mathbf{12}] \tag{1.13}$$

$$[\mathbf{12}] = f([\mathrm{LiHMDS}], [\mathbf{1}]_{\mathrm{total}}, [\mathrm{DMEA}], [\mathrm{toluene}]) \tag{1.14}$$

$$\underset{\mathbf{12}}{\mathrm{A_2(DMEA)(\mathbf{1})}} \xrightarrow{k'} \underset{\boldsymbol{E}\textbf{-17}}{[\mathrm{A_2(DMEA)(\mathbf{1})}]^{\ddagger}} \tag{1.15}$$

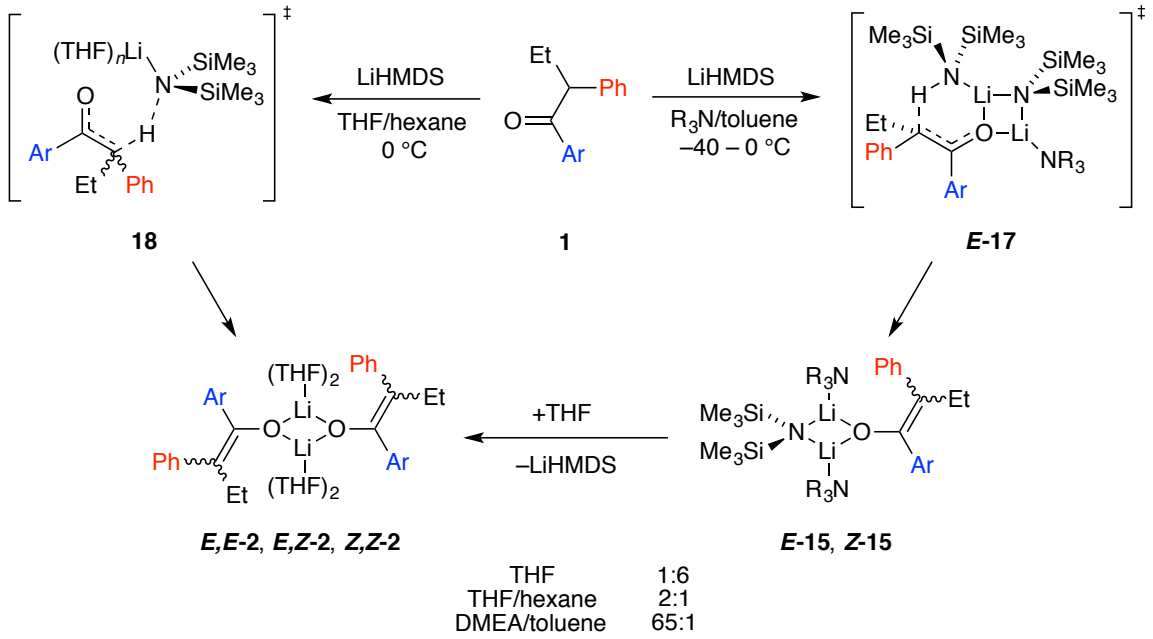
Discussion

Tetrasubstituted alkene moieties as central motifs of GDC-0810 and a number of key anticancer agents pose particularly daunting synthetic challenges.[1–4] The potentially general solution to the problem presented in Scheme 1.1 is notable, yet the mediocre stereoselectivity obtained using LiHMDS/THF for the enolization of **1** underscores a central challenge. LiHMDS in DMEA/toluene solves the problem of stereoselectivity. Reversing the roles of the Ar and Ph moieties offers the final puzzle piece—full stereo*control*.[5]

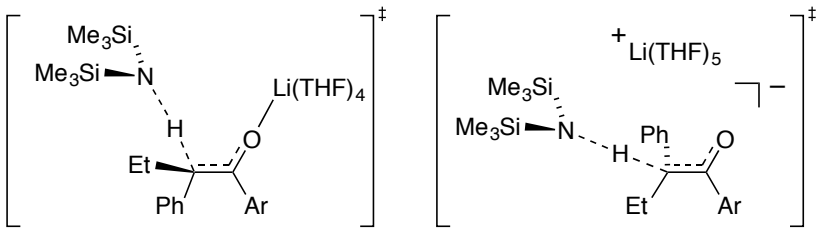
Structural and mechanistic studies of the enolizations are summarized in Scheme 1.1. Enolization with LiHMDS in neat THF affords an ensemble of ***E,E*-2**, ***E,Z*-2**, and ***Z,Z*-2** dimeric

enolates that reflect the 1:6 *E/Z* selectivity confirmed by the trapping with Ts_2O described in a previous paper.[5] Reduced THF concentrations reverse the selectivity, promoting a slight (2:1) preference for ***E*-2**. The results of rate studies reveal that the *E* selectivity stems from a dominant *tetrasolvated*-monomer-based pathway, whereas the *Z* selectivity arises from a *pentasolvated*-monomer-based pathway. The different selectivities may originate from closed and open transition structures (respectively) or even contact- and solvent-separated ion pairs, but such highly solvated systems defy scrutiny with DFT methods. Attempts to compute transition structures with lower solvation numbers (**18**, n = 1–3) were not predictive and are relegated to the supporting information. Structures **18a** and **18b** are merely artists' renditions. We also hasten to add that minor contributions from other solvates could easily go undetected, but the THF-concentration-dependent change in selectivity stems primarily from a differential solvation of only one THF (see Figure 1.4).

Scheme 1.3. Summary of mechanisms for the enolization of ketone **1** using LiHMDS.

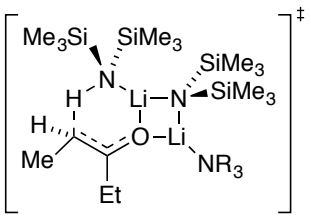


Previous studies showed that LiHMDS in trialkylamine/hydrocarbon mixtures enolize simple ketones (eq 1.1) with extraordinarily high selectivity via a dimer-based pathway suggested by MNDO computations to be **6**.[8] Indeed, the enolization of **1** with LiHMDS/DMEA or LiHMDS/Et_3N afforded what may be an even more extraordinary 65:1 *E/Z* selectivity. The resulting enolates in poorly coordinating trialkylamines form mixed aggregates ***E*-15** and ***Z*-15** in proportions consistent with trapping experiments.[5] Adding THF converted the mixed aggregates to an ensemble of dimers dominated by homodimer ***E,E*-2**.



18a **18b**

The results of structural and mechanistic studies using Et_3N show that ketone complex **11** is *not* observably solvated to form **12**. However, rate study findings clearly implicate monosolvated-dimer-based transition structure ***E*-17** analogous to results with the less congested ketones.[8] The developing mixed dimer motif in ***E*-17**—the developing transannular Li–O contact—was observed computationally to the exclusion of the 8-membered ring depicted in **6**. We reinvestigated **6** with 3-pentanone using DFT and found that the transition structure converged on the closed motif ***E*-19** analogous to ***E*-17**. In all cases, intrinsic reaction coordinate calculations in the reverse direction reveal a lengthening on the transannular Li–O contact toward a structure resembling that of **6**.



***E*-19**

This summary seems neat and tidy and almost simple, but the structural and mechanistic complexity should not be underestimated. Ketone complex **11** is readily converted to the corresponding solvate **12** at low concentrations of the relatively unhindered DMEA. Elevated DMEA concentrations, however, deaggregate **12** to form LiHMDS monomer with the concomitant liberation of free ketone. Moreover, LiHMDS deaggregation is remarkably sensitive to the choice of hydrocarbon cosolvent, as noted previously for LiHMDS/*N*,*N*-diethylmethylamine. In DMEA/hexane, the sole observable monomer is trisolvate **14**. Toluene, by contrast, stabilizes the monomer and promotes deaggregation and decomplexation owing to the intervention of disolvated monomer **13** stabilized by a molecule of toluene. Whether toluene is explicitly bound is unknowable, but the fit to an explicit solvate is excellent.

At this point, the data analysis becomes gruesome. Although parallel pathways from a common ground state are readily deconvoluted, we are just beginning to develop the numerical skills to model systems with multiple condition-dependent reactants.[20] The fit in Figure 1.10, for example, is based on a complex equation crudely outlined in eqs 1.13–1.15 and described thoroughly in the supporting information. The slight upward curvature at high DMEA concentrations in Figure 1.10 stems from contributions by the toluene-solvated monomer. The model includes provisions for simple dependencies in the other figures as well.

We highlight a key observation about the role of aggregate-based reactivity for LiHMDS/DMEA. In neat DMEA, the dominant form of LiHMDS is trisolvated LiHMDS monomer **14** uncomplexed by ketone; however, highly *E*-selective enolization and saturation kinetics (see Figure 1.12) show that the preferred pathway involves *reaggregation* to complexed

dimer **12** (observable at the saturation plateau) and enolization via dimer-based transition structure ***E*-17**. The notion that a monomer would *reaggregate* to react seems blasphemous, but evidence supporting such processes has begun to accumulate (including a LiHMDS/THF-mediated enolization).[12b,20,23]

Conclusion

The preceding analyses presented a particularly interesting problem in which a pharmaceutical need for an acutely challenging stereoselective enolization aligned with an academic interest in solvation and aggregation effects on enolizations. The application of LiHMDS/trialkylamine mixtures to enolizations have been largely (although not entirely) of academic interest until now. LiHMDS in trialkylamine-hydrocarbon mixtures is a highly efficacious, cost-effective base-solvent combination.

The notion that stereoselectivity stems from (at least) two discrete pathways is a truism with implications that can be overlooked. The idea that selectivity can be controlled by diverting a monomer-based enolization to a dimer-based pathway or by merely decreasing the solvation number by a single solvent is more nuanced. To this end, we emphasize that it is not only constructive to vary solvents during optimizations but also to vary solvent *concentration*s and even the hydrocarbon cosolvent.[12a]

Experimental

Reagents and solvents. THF, toluene, hexane, and the trialkylamines were distilled from blue or purple solutions containing sodium benzophenone ketyl. LiHMDS, [^{6}Li]LiHMDS, and [^{6}Li,^{15}N]LiHMDS were prepared as ligand- and LiCl-free recrystallized solids.[9] Ketone **1** was prepared as described in a preceding paper.[5] Air- and moisture-sensitive materials were manipulated under argon using standard glovebox, vacuum line, and syringe techniques.

2-Deutero-1-(4-fluorophenyl)-2-phenylbutan-1-one (1-*d*$_1$). Following a literature procedure,[24] we charged a small vial with 1.0 g of **1** in 2.5 mL MeOD under positive argon flow.

To the vial was added 1.0 mL of 2.60 M NaOD/D_2O. The solution was stirred for 30 min. The vial was opened, and 35% DCl was added until the solution was neutralized. Three extractions were performed with pentane, followed by solvent removal in vacuo. The oil was further purified via column chromatography (10% ether/pentane) to afford 0.86 grams **1-*d*$_1$** (86% yield) as a clear, slightly yellow oil. The results of ^{1}H NMR spectroscopy and gas chromatography-mass spectroscopy showed >99% **1–*d*$_1$**.

IR spectroscopic analyses. IR spectra were recorded using an in situ IR spectrometer fitted with a 30-bounce, silicon-tipped probe. The spectra were acquired in 16 scans at a gain of 1 and a resolution of 4 cm^{-1}. A representative reaction was carried out as follows: The IR probe was inserted through a nylon adapter and O-ring seal into an oven-dried, cylindrical flask fitted with a magnetic stir bar and a T-joint. The T-joint was capped with a septum for injections and a nitrogen line. After evacuation under full vacuum, heating, and flushing with nitrogen, the flask was charged with LiHMDS (84 mg, 0.50 mmol) in THF/hexane (4.9 mL total volume) and cooled to 0 °C with a stirred ice bath. After recording a background spectrum, we added ketone **1** (0.050 mmol in 0.10 mL) with stirring. The carbonyl absorbance at 1687 cm^{-1} was monitored over the course of the reaction.

NMR spectroscopic analyses. All NMR samples for reaction monitoring and structure elucidation were prepared using stock solutions and sealed under partial vacuum. Standard ^{1}H, ^{6}Li, ^{13}C, and ^{15}N NMR spectra were recorded at 500, 73.6, 126, and 36.1 MHz, respectively

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I. NMR Spectroscopic Studies

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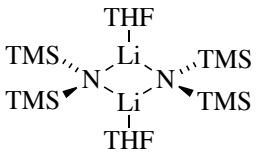
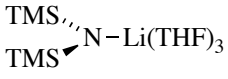
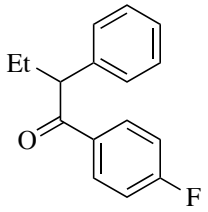
Species	δ (ppm)
A_2S_2	1.16
AS_3	0.18
EE	0.19
EZ	0.03
ZZ	–0.13



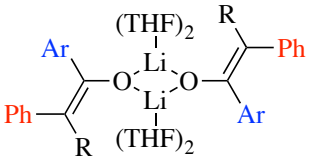
A_2S_2



AS_3



ketone



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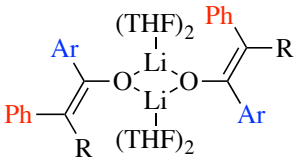

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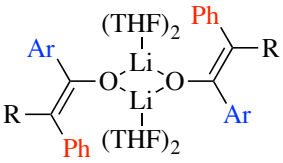

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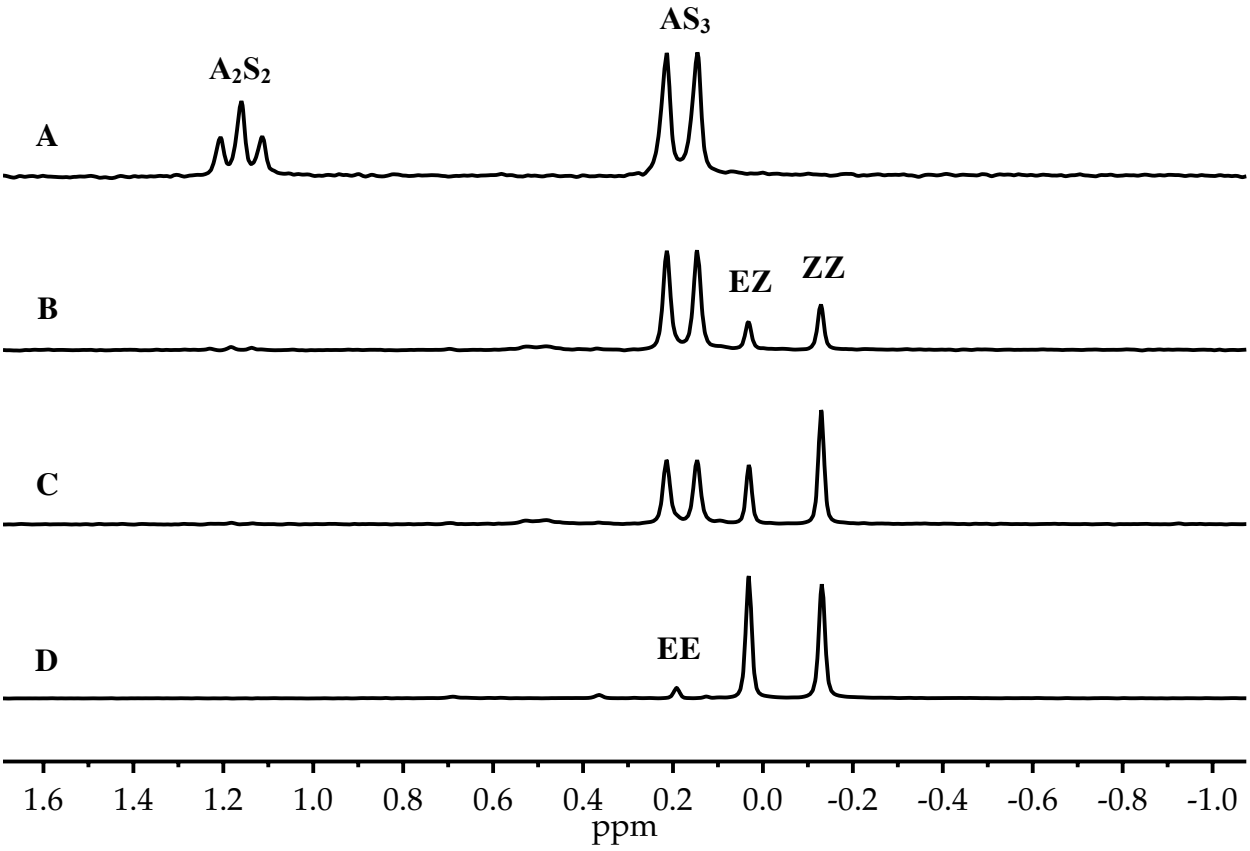


Figure A.1.1. ^{6}Li spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS with varying amounts of ketone in neat THF at –80 °C after aging at rt for 1 h: a) No ketone, 0.10 M LiHMDS in 6.0 M THF/hex; b) 0.020 M ketone; c) 0.050 M ketone; d) 0.10 M ketone. This figure shows the independence of E/Z selectivity on the LiHMDS:ketone ratio.

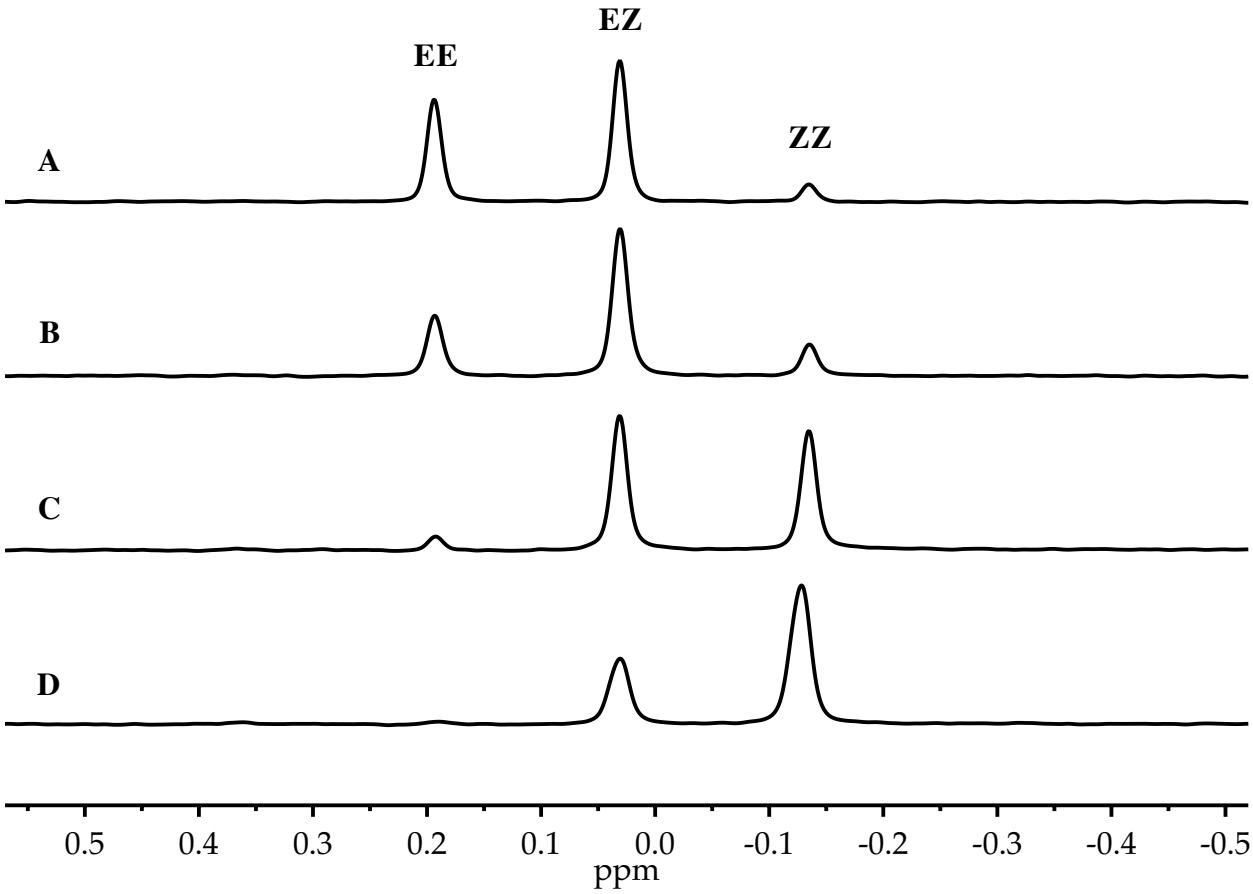


Figure A.1.2. ^{6}Li spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS and 0.10 M ketone with varying amounts of THF in hexane cosolvent at –80 °C after aging at rt for 48 h: a) 3.0 M THF/hex; b) 4.5 M THF/hex; c) 6.0 M THF/hex; d) neat THF. This figure shows the dependence of E/Z selectivity on the concentration of THF.

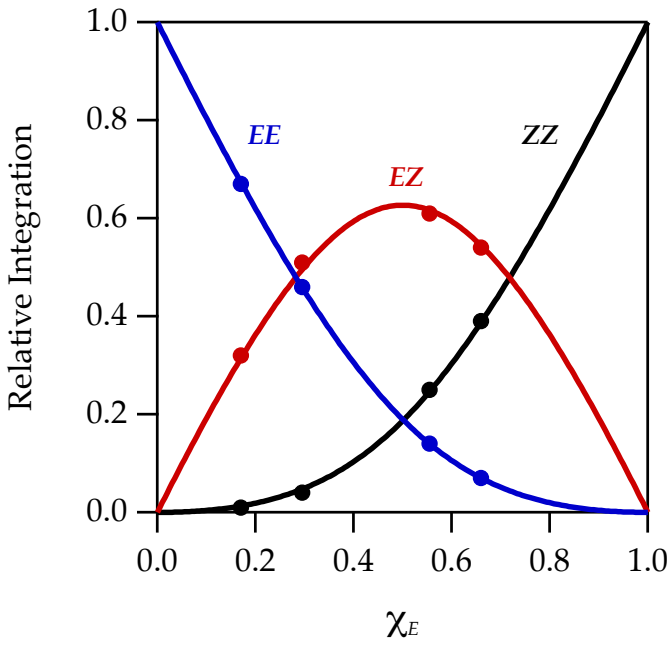
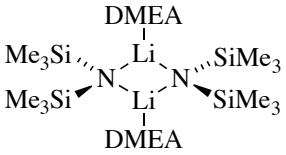


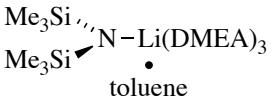
Figure A.1.3. Job plot showing the relative integration of the ^{6}Li resonances versus the measured mole fraction ($X_{\boldsymbol{E}}$) of ***E***-enolate for 0.10 M mixtures of ***E***-enolate and ***Z***-enolate at –80 °C at varying THF concentrations in hexane (see Figure A.1.2).

Table A.1.2. ^{6}Li and ^{15}N NMR chemical shifts for different species in 0.60 M DMEA/toluene at –100 °C. Note that species without chemical shifts could not be characterized at the given temperature due weak signal.

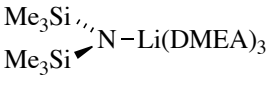
Species	^{6}Li δ (ppm) at –100 °C	^{15}N δ (ppm) at –100 °C
A_2S_2	0.64	40.00
AS_2T/AS_3	0.36	46.10
A_2S(ketone)	0.85, 1.24	39.90
A_2(ketone)$_2$	1.43	40.44
AES_2	0.64	41.88
AZS_2	0.50	–



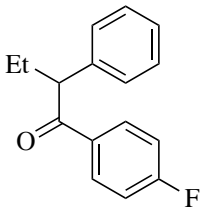
A_2S_2



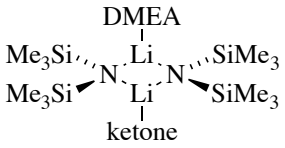
AS_2T



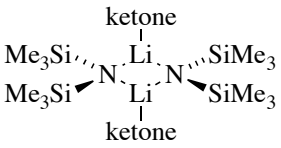
AS_3



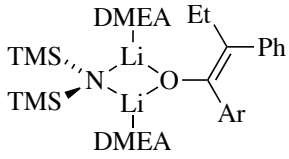
ketone



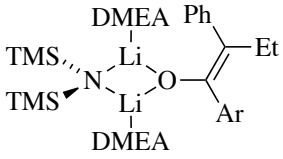
A_2(ketone)



A_2(ketone)$_2$



AES_2



AZS_2

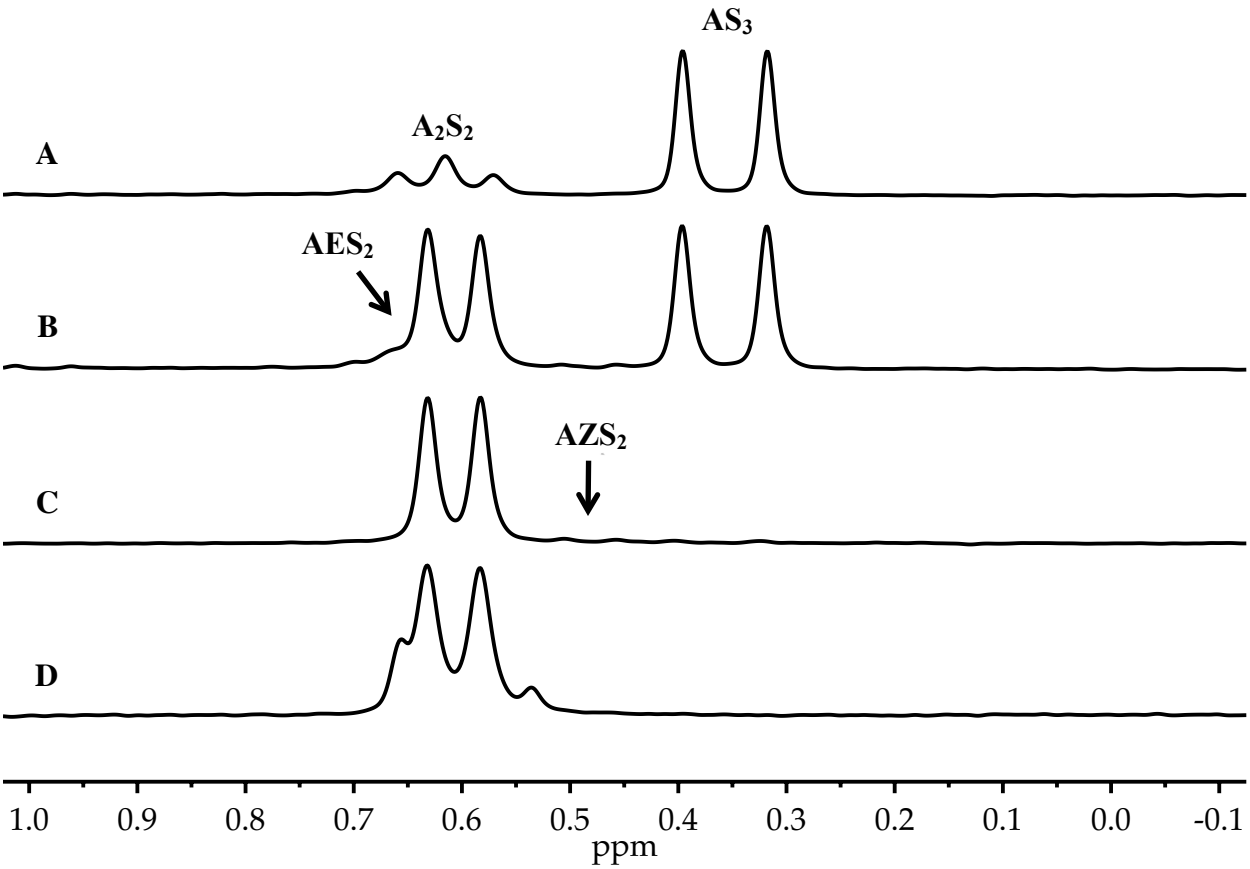


Figure A.1.4. ^{6}Li spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS with varying amounts of ketone in 0.60 M DMEA/tol at –80 °C after aging at rt for 1 h: a) No ketone; b) 0.020 M ketone; c) 0.050 M ketone; d) 0.10 M ketone.

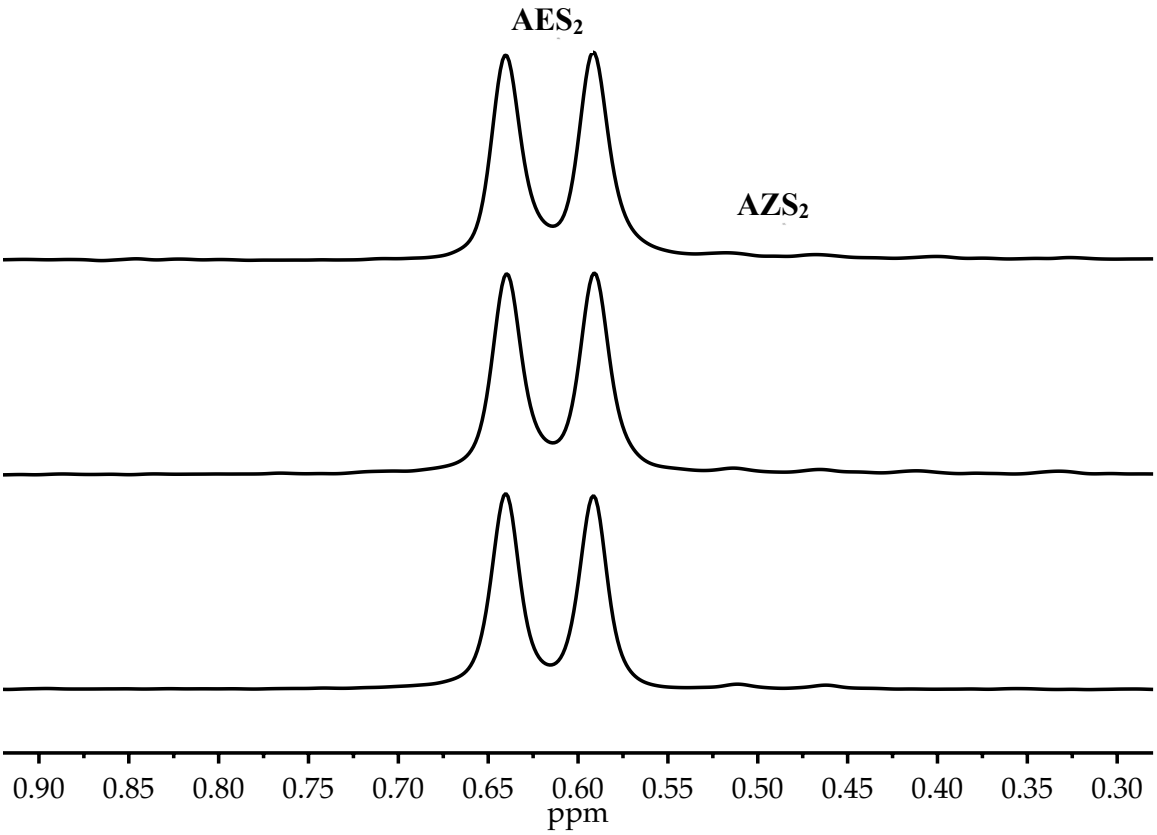


Figure A.1.5. ^{6}Li spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS and 0.050 M ketone with varying amounts of DMEA in toluene cosolvent at –80 °C after aging at rt for 1 h: a) 0.60 M DMEA/tol; b) 1.1 M DMEA/tol; c) 5.1 M DMEA/tol.

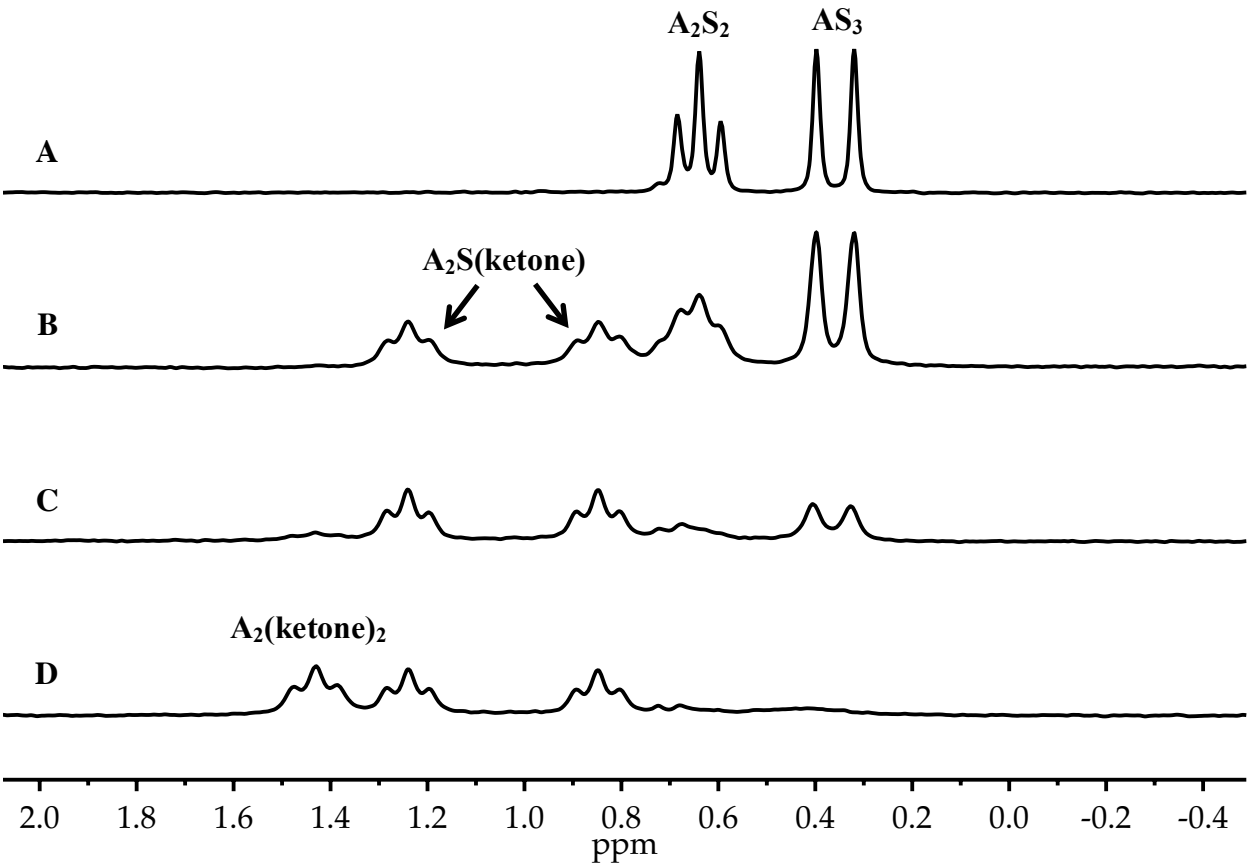


Figure A.1.6. Unaged ^{6}Li spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS with varying amounts of ketone in 0.60 M DMEA/tol at –100 °C: a) No ketone; b) 0.020 M ketone; c) 0.050 M ketone; d) 0.10 M ketone.

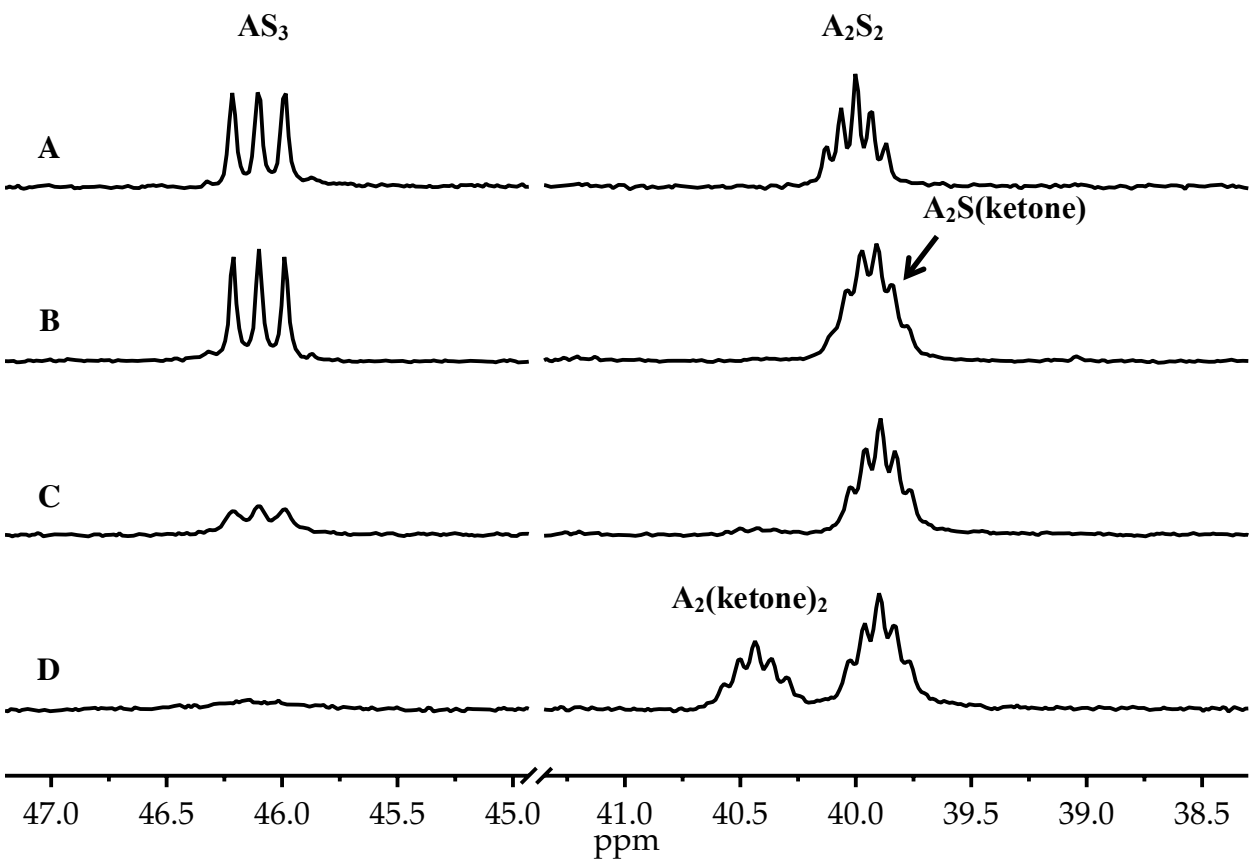


Figure A.1.7. Unaged ^{15}N spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS with varying amounts of ketone in 0.60 M DMEA/tol at –100 °C: a) No ketone; b) 0.020 M ketone; c) 0.050 M ketone; d) 0.10 M ketone.

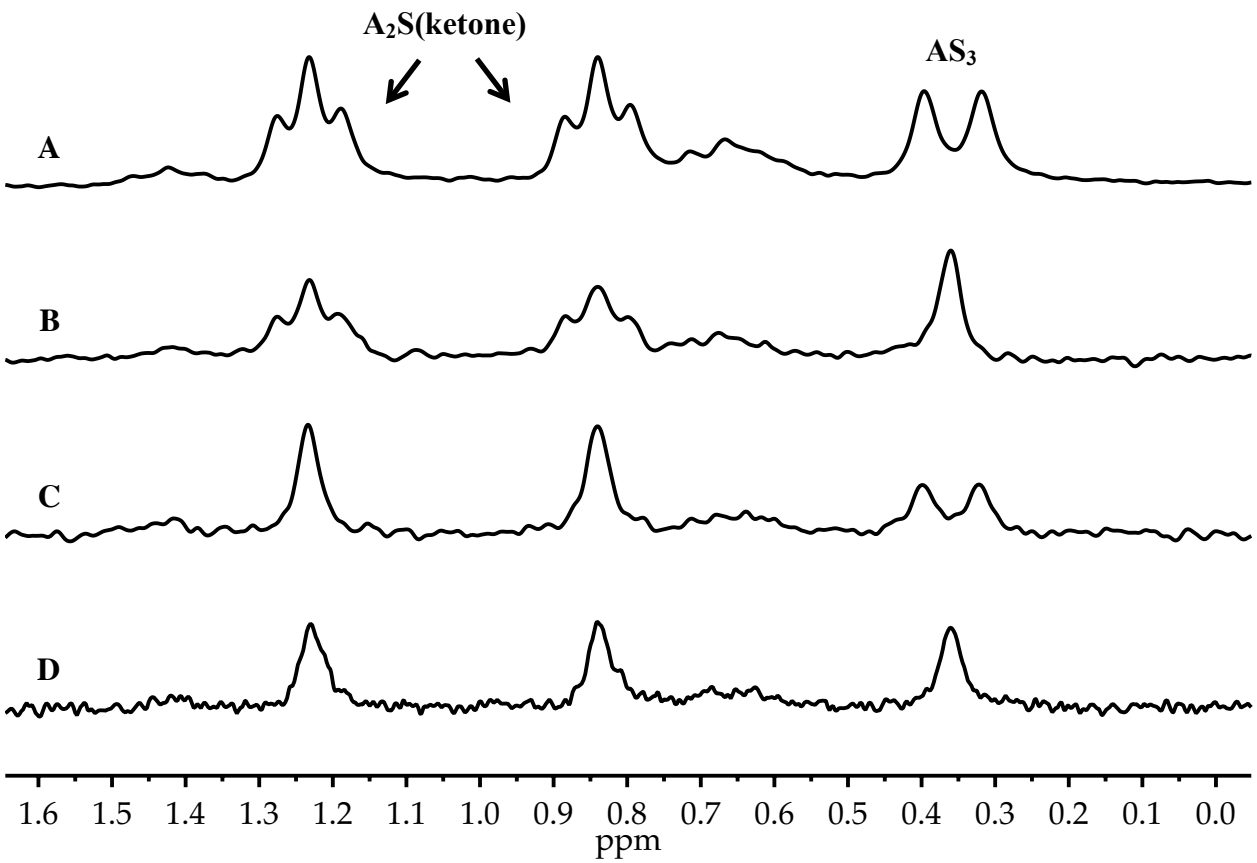


Figure A.1.8. ^{15}N-decoupled unaged ^{6}Li spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS with 0.050 M ketone in 0.60 M DMEA/tol at –100 °C: a) fully coupled; b) selective decoupling of ^{15}N resonance corresponding to LiHMDS monomer at 46.10 ppm; c) selective decoupling of ^{15}N resonance at 39.90 ppm; d) broadband decoupled.

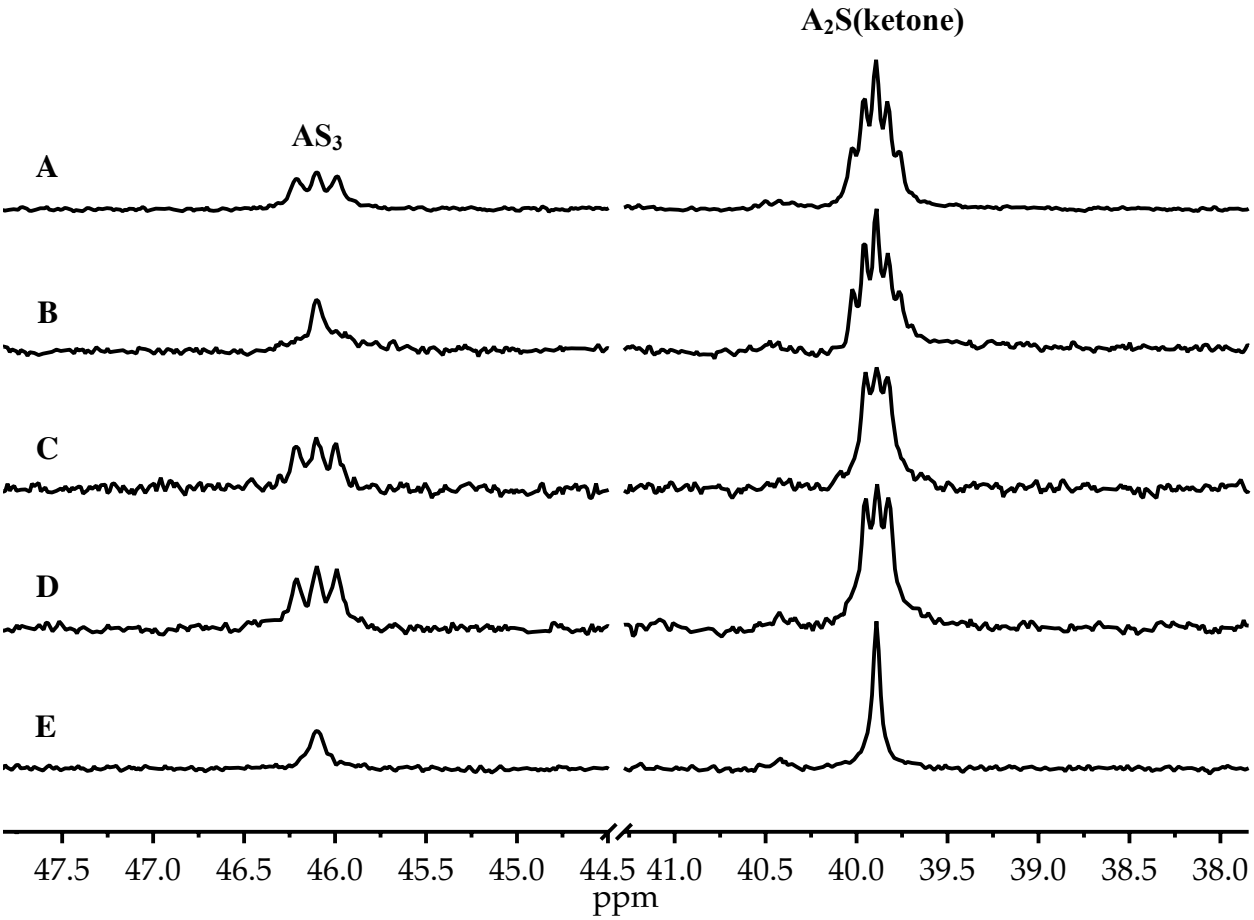


Figure A.1.9. ^{6}Li-decoupled unaged ^{15}N spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS with 0.10 M ketone in 0.60 M DMEA/tol at –100 °C: a) fully coupled; b) selective decoupling of ^{6}Li resonance corresponding to LiHMDS monomer at 0.36 ppm; c) selective decoupling of the upfield ^{6}Li resonance at 0.85 ppm; d) selective decoupling of the downfield ^{6}Li resonance at 1.24 ppm; e) broadband decoupled.

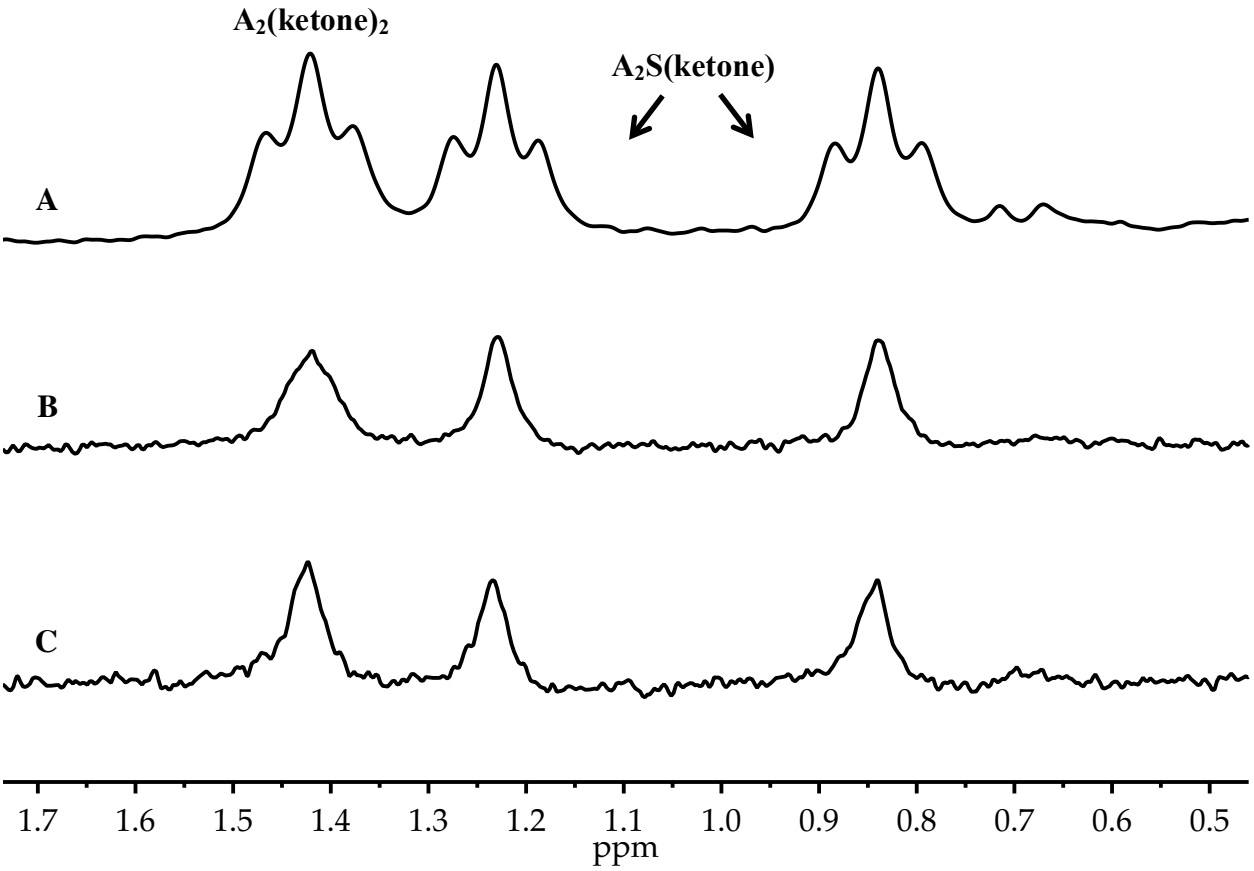


Figure A.1.10. ^{15}N-decoupled unaged ^{6}Li spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS with 0.050 M ketone in 0.60 M DMEA/tol at –100 °C: a) fully coupled; b) selective decoupling of ^{15}N resonance at 39.90 ppm; c) broadband decoupled. Note that the downfield triplet in spectrum b is independent of the two upfield triplets. The loss of coupling is due to the closeness of the ^{15}N resonances corresponding to the mono- and di-ketone-solvated LiHMDS dimers (39.90 and 40.44 ppm, respectively).

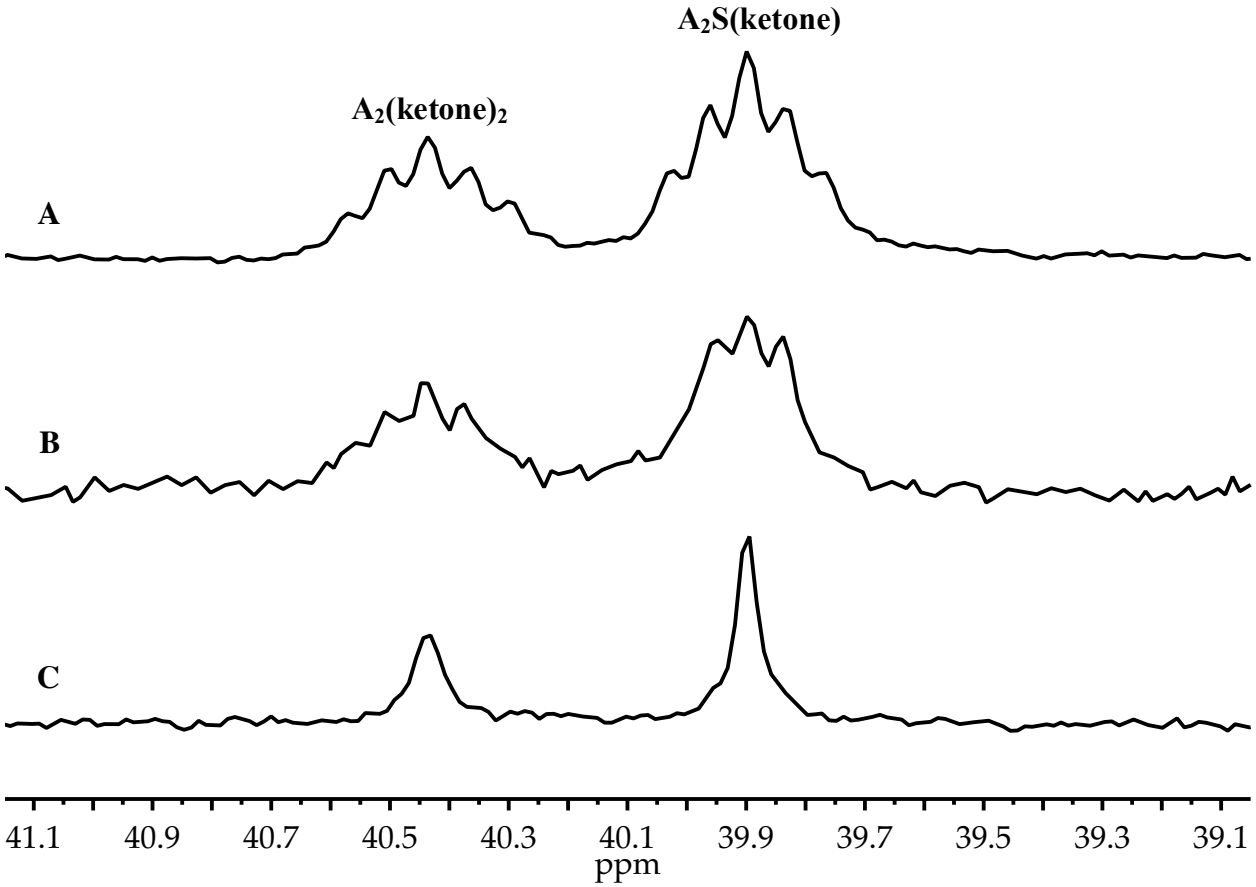


Figure A.1.11. ^{6}Li-decoupled unaged ^{15}N spectra of 0.10 M [^{6}Li,^{15}N]LiHMDS with 0.10 M ketone in 0.60 M DMEA/tol at –100 °C: a) fully coupled; b) selective decoupling of ^{6}Li resonance at 0.85 ppm; c) broadband decoupled. Note that the downfield quintet in spectrum b is independent of the upfield quintet. The loss of coupling is due to the closeness of the ^{6}Li resonances corresponding to the mono- and di-ketone-solvated LiHMDS dimers (1.24 and 1.43 ppm, respectively).

II. IR Rate Studies

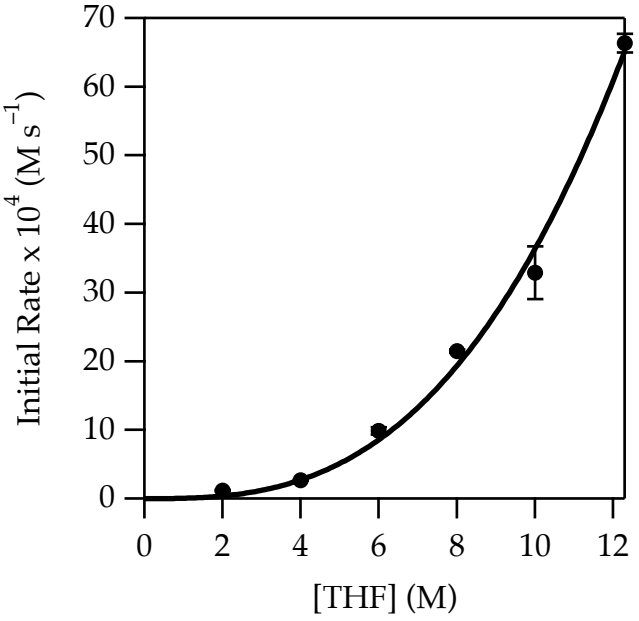


Figure A.1.12. Plot of initial rate vs. THF concentration in toluene for the enolization of **1** (0.010 M) by LiHMDS (0.10 M) at 0 °C measured with IR spectroscopy (1687 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 0.05 \pm 0.03$, $n = 2.8 \pm 0.2$).

[THF] (M)	Initial rate[1] × 10^4 ($M\ s^{-1}$)	Initial rate[2] × 10^4 ($M\ s^{-1}$)	Initial Rate[avg] × 10^4 ($M\ s^{-1}$)
2.0	1.131	1.249	1.19 ± 0.08
4.0	2.695	2.619	2.66 ± 0.05
6.0	9.462	10.235	9.8 ± 0.5
8.0	21.319	21.678	21.5 ± 0.3
10.0	35.616	30.168	33 ± 4
12.3	65.424	67.317	66 ± 1

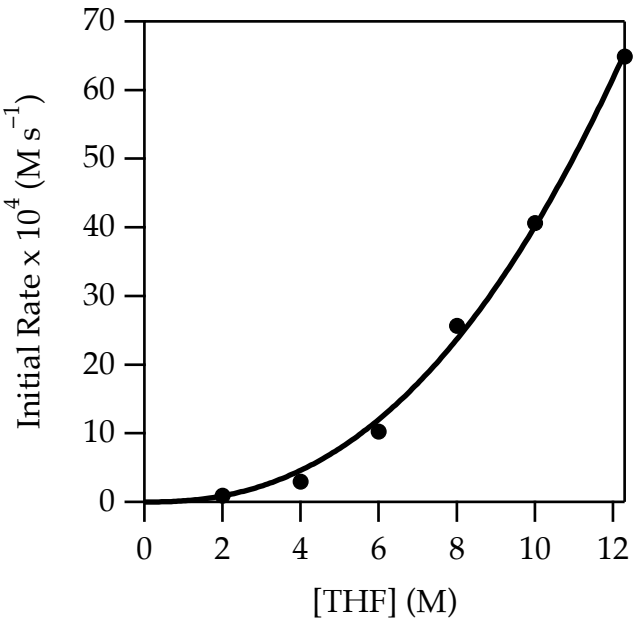


Figure A.1.13. Plot of initial rate vs. THF concentration in toluene for the enolization of **1** (0.010 M) by LiHMDS (0.10 M) at 0 °C measured with IR spectroscopy (1687 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 0.18 \pm 0.05$, $n = 2.4 \pm 0.1$).

[THF] (M)	Initial rate × 10^4 ($M\ s^{-1}$)
2.0	0.914
4.0	2.941
6.0	10.25
8.0	25.680
10.0	40.663
12.3	64.890

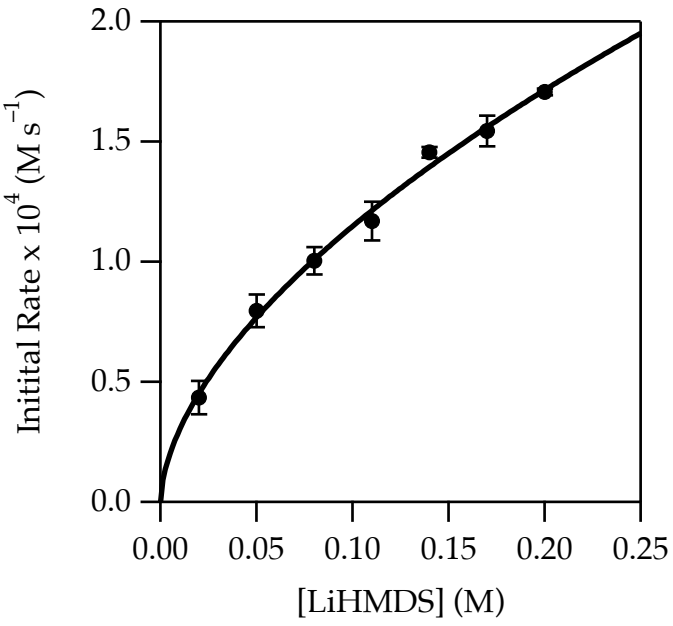


Figure A.1.14. Plot of initial rate vs. LiHMDS concentration in 2.0 M THF/hexane for the enolization of **1** (0.010 M) at 0 ºC measured with IR spectroscopy (1687 cm^{-1}). The curve depicts an unweighted least-squares fit to $y = ax^n$ [$a = 4.4 \pm 0.2$, $n = 0.58 \pm 0.02$].

[LiHMDS] (M)	Initial rate[1] × 10^4 ($M\ s^{-1}$)	Initial rate[2] × 10^4 ($M\ s^{-1}$)	Initial Rate[avg] × 10^4 ($M\ s^{-1}$)
0.020	0.385	0.484	0.43 ± 0.07
0.050	0.748	0.843	0.80 ± 0.07
0.080	1.044	0.963	1.00 ± 0.06
0.110	1.227	1.113	1.17± 0.08
0.140	1.439	1.472	1.46 ± 0.02
0.170	1.589	1.499	1.54 ± 0.06
0.200	1.697	1.718	1.71 ± 0.01

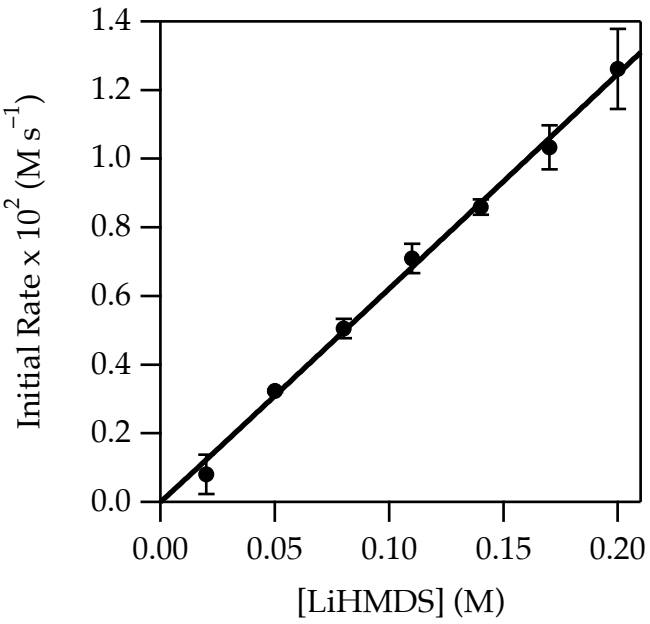


Figure A.1.15. Plot of initial rate vs. LiHMDS concentration in neat THF (12.2M) for the enolization of **1** (0.010 M) at 0 ºC measured with IR spectroscopy (1687 cm^{-1}). The curve depicts an unweighted least-squares fit to $y = ax^n$ [$a = 6.3 \pm 0.5$, $n = 1.01 \pm 0.04$].

[LiHMDS] (M)	Initial rate[1] × 10^2 ($M\ s^{-1}$)	Initial rate [2] × 10^2 ($M\ s^{-1}$)	Initial Rate[avg] × 10^2 ($M\ s^{-1}$)
0.020	0.121	0.0397	0.080 ± 0.06
0.050	0.326	0.321	0.323 ± 0.004
0.080	0.526	0.486	0.51 ± 0.03
0.110	0.740	0.679	0.71 ± 0.04
0.140	0.844	0.876	0.86 ± 0.02
0.170	1.079	0.988	1.03 ± 0.06
0.200	1.179	1.344	1.3 ± 0.1

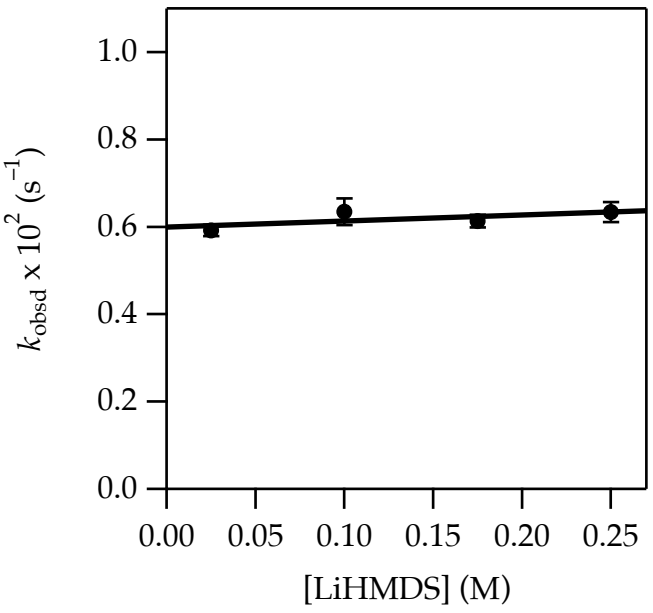


Figure A.1.16. Plot of k_{obsd} vs. LiHMDS concentration in 1.10 M Et_3N/toluene for the enolization of **1** (0.0025 M) at 0 ºC measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to y = ax + b [a = 0.60 ± 0.02, b = 0.1 ± 0.1].

[LiHMDS] (M)	$k_{obsd}^{1} \times 10^2$ (s^{-1})	$k_{obsd}^{2} \times 10^2$ (s^{-1})	$k_{obsd}^{avg} \times 10^2$ (s^{-1})
0.025	0.581	0.602	0.59 ± 0.01
0.100	0.614	0.656	0.64 ± 0.03
0.175	0.622	0.606	0.61 ± 0.01
0.250	0.619	0.648	0.63 ± 0.02

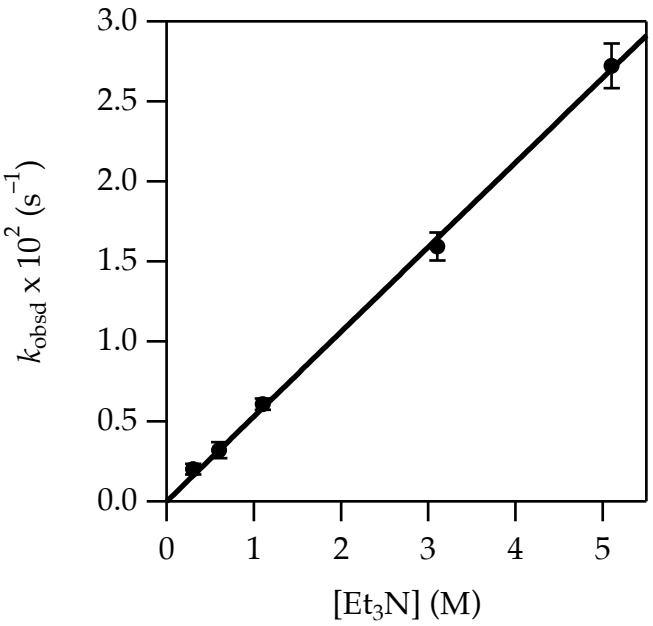


Figure A.1.17. Plot of k_{obsd} vs. Et_3N concentration in toluene for the enolization of **1** (0.0050 M) with LiHMDS (0.10 M) at 0 °C measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to $y = ax^n$ [$a = 0.53 \pm 0.03$, $n = 1.00 \pm 0.03$].

[Et_3N] (M)	$k_{obsd}^1 \times 10^2$ (s^{-1})	$k_{obsd}^2 \times 10^2$ (s^{-1})	$k_{obsd}^{avg} \times 10^2$ (s^{-1})
0.30	0.215	0.175	0.20 ± 0.03
0.60	0.366	0.289	0.33 ± 0.05
1.10	0.645	0.582	0.61 ± 0.04
3.10	1.675	1.543	1.61 ± 0.09
5.10	2.617	2.802	2.7 ± 0.1

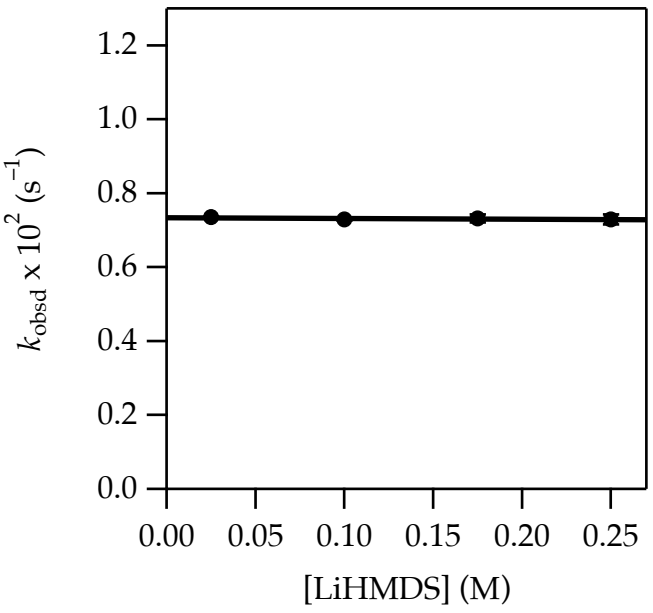


Figure A.1.18. Plot of k_{obsd} vs. LiHMDS concentration in 1.10 M Et_3N/hexane for the enolization of **1** (0.0025 M) at 0 ºC measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to y = ax + b [a = 0.734 ± 0.003, b = –0.02 ± 0.02].

[LiHMDS] (M)	$k_{obsd}^{1} \times 10^2$ (s^{-1})	$k_{obsd}^{2} \times 10^2$ (s^{-1})	$k_{obsd}^{avg} \times 10^2$ (s^{-1})
0.025	0.735	0.736	0.7354 ± 0.0006
0.100	0.727	0.731	0.729 ± 0.003
0.175	0.740	0.725	0.73 ± 0.01
0.250	0.720	0.738	0.73 ± 0.01

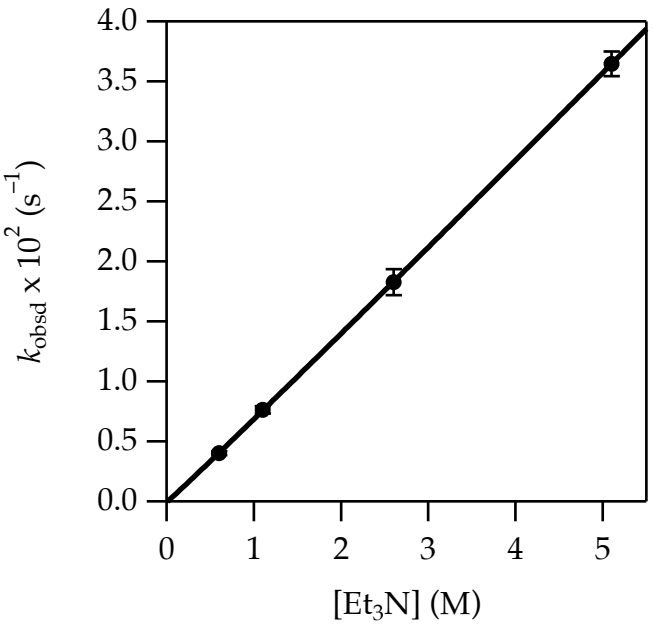


Figure A.1.19. Plot of k_{obsd} vs. Et_3N concentration in hexane for the enolization of **1** (0.0050 M) with LiHMDS (0.10 M) at 0 °C measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to $y = ax^n$ [$a = 0.69 \pm 0.01$, $n = 1.02 \pm 0.01$].

[Et_3N] (M)	$k_{obsd}^1 \times 10^2$ (s^{-1})	$k_{obsd}^2 \times 10^2$ (s^{-1})	$k_{obsd}^{avg} \times 10^2$ (s^{-1})
0.60	0.391	0.414	0.40 ± 0.02
1.10	0.743	0.785	0.76 ± 0.03
2.60	1.904	1.752	1.8 ± 0.1
5.10	3.575	3.720	3.6 ± 0.1

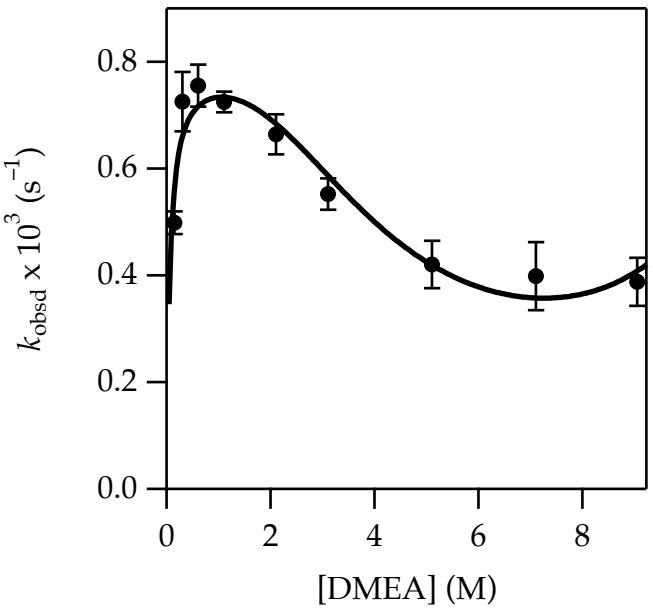


Figure A.1.20. Plot of k_{obsd} vs. DMEA concentration with toluene cosolvent for the enolization of **1** (0.0050 M) by LiHMDS (0.10 M) at –40 °C measured with IR spectroscopy (1671 cm^{-1}). The curve is fit to the function described in the "Derivations" section of this appendix on page 59. [$a_0 = 0.1$, $k_0 = 0.005$, $k_1 = 20$, $k_2 = 0.00005$, $k_{g1} = 0.2$, $k_{g2} = 0.044$, $k_{g3} = 0.0581$, kk = 158].

[DMEA] (M)	$k_{obsd}^1 \times 10^3$ (s^{-1})	$k_{obsd}^2 \times 10^3$ (s^{-1})	$k_{obsd}^{avg} \times 10^3$ (s^{-1})
0.15	0.519	0.484	0.50 ± 0.02
0.30	0.768	0.686	0.73 ± 0.06
0.60	0.728	0.783	0.76 ± 0.04
1.10	0.711	0.739	0.73 ± 0.02
2.10	0.692	0.633	0.66 ± 0.04
3.10	0.522	0.569	0.55 ± 0.03
5.10	0.452	0.397	0.42 ± 0.04
7.10	0.446	0.355	0.40 ± 0.06
9.05	0.424	0.362	0.39 ± 0.04

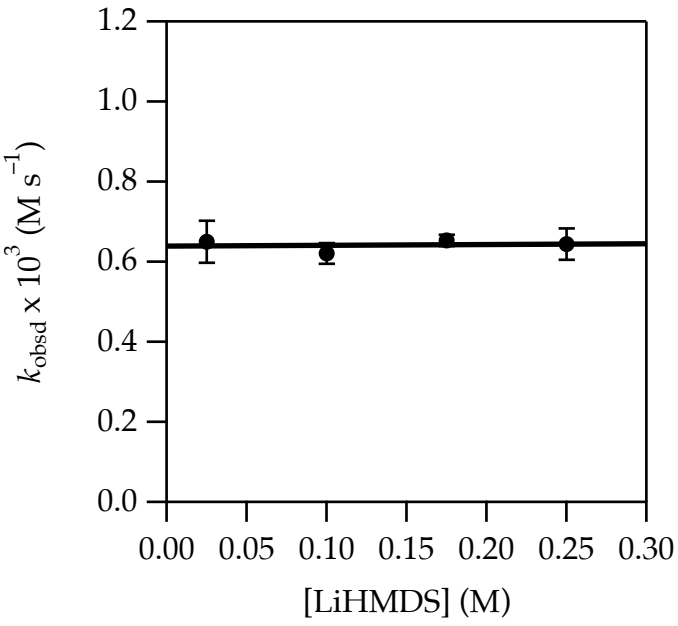


Figure A.1.21. Plot of k_{obsd} vs. LiHMDS concentration in 0.60 M DMEA/toluene for the enolization of **1** (0.0025 M) at –40 ºC measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to y = ax + b [a = 0.64 ± 0.02, b = 0.2 ± 0.1].

[LiHMDS] (M)	$k_{obsd}^1 \times 10^3$ (s^{-1})	$k_{obsd}^2 \times 10^3$ (s^{-1})	$k_{obsd}^{avg} \times 10^3$ (s^{-1})
0.025	0.688	0.613	0.65 ± 0.05
0.100	0.603	0.639	0.62 ± 0.03
0.175	0.643	0.663	0.65 ± 0.01
0.250	0.616	0.672	0.64 ± 0.04

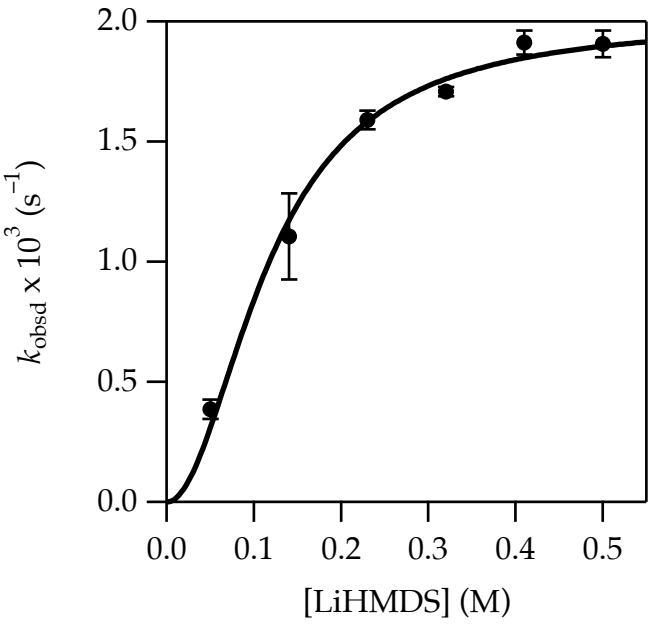


Figure A.1.22. Plot of k_{obsd} vs. LiHMDS concentration in neat DMEA (9.2 M) for the enolization of **1** (0.0050 M) at –40 °C measured with IR spectroscopy (1687 cm^{-1}). The curve is fit to the function described in the "Derivations" section of this appendix on page 59. [a_0 = 0.1, k_0 = 0.005, k_1 = 20, k_2 = 0.00008, k_{g1} = 0.2, k_{g2} = 0.044, k_{g3} = 0.0581, kk = 405 ± 6)

[DMEA] (M)	$k_{obsd}^1 \times 10^3$ (s^{-1})	$k_{obsd}^2 \times 10^3$ (s^{-1})	$k_{obsd}^{avg} \times 10^3$ (s^{-1})
0.050	0.358	0.415	0.39 ± 0.04
0.125	0.978	1.232	1.1 ± 0.2
0.225	1.562	1.615	1.59 ± 0.04
0.300	1.721	1.692	1.71 ± 0.02
0.400	1.878	1.947	1.91 ± 0.05
0.500	1.868	1.957	1.91 ± 0.06

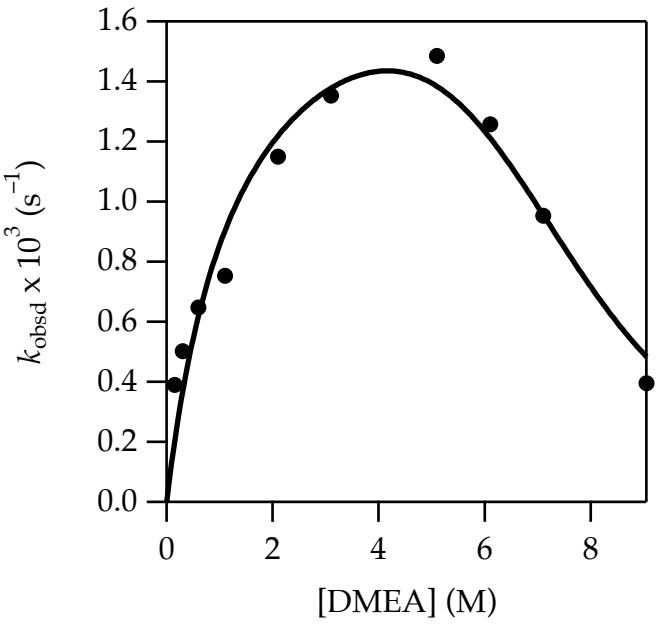


Figure A.1.23. Plot of k_{obsd} vs. DMEA concentration with hexane cosolvent for the enolization of **1** (0.0050 M) by LiHMDS (0.10 M) at –40 °C measured with IR spectroscopy (1671 cm^{-1}). The curve is fit to the function described in the "Derivations" section of this appendix on page 56. [$a_0 = 0.1$, $k_0 = 0.005$, $k_1 = 20$, $k_2 = 0.00005$, $k_{g1} = 0.2$, $k_{g2} = 0.044$, $k_{g3} = 0.0581$, kk = 158].

[DMEA] (M)	$k_{obsd} \times 10^3$ (s^{-1})
0.15	0.390
0.30	0.502
0.60	0.648
1.10	0.754
2.10	1.150
3.10	1.353
5.10	1.486
6.10	1.257
7.10	0.954
9.05	0.396

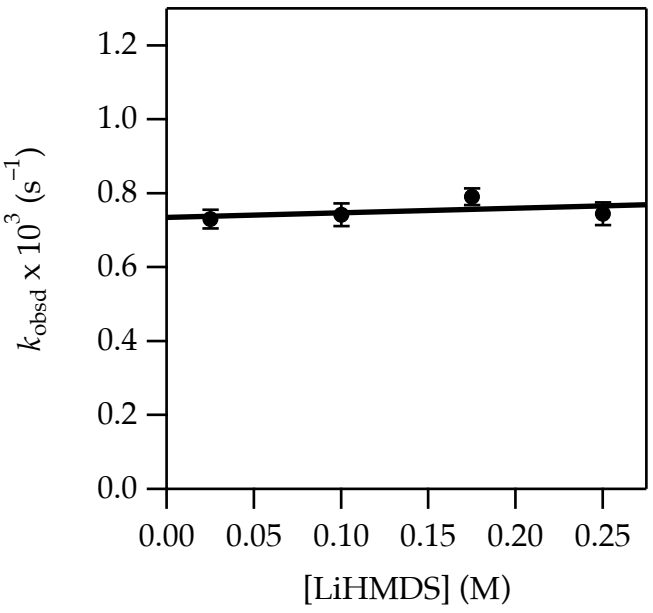


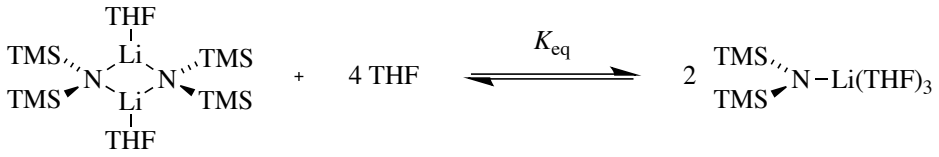
Figure A.1.24. Plot of k_{obsd} vs. LiHMDS concentration in 0.60 M DMEA/hexane for the enolization of **1** (0.0025 M) at –40 ºC measured with IR spectroscopy (1671 cm^{-1}). The curve depicts an unweighted least-squares fit to y = ax + b [a = 0.74 ± 0.02, b = 0.12 ± 0.02].

[LiHMDS] (M)	$k_{obsd}^{1} \times 10^3$ (s^{-1})	$k_{obsd}^{2} \times 10^3$ (s^{-1})	$k_{obsd}^{avg} \times 10^3$ (s^{-1})
0.025	0.749	0.711	0.730
0.100	0.724	0.761	0.742
0.175	0.808	0.773	0.791
0.250	0.722	0.769	0.745

III. Derivations

D.A.1.1. LiHMDS-mediated enolization: THF

To simplify the discussion of the mechanistic model, we introduce the following shorthand: A = a LiHMDS subunit, and S = THF. As shown below, A_2S_2 corresponds to disolvated LiHMDS dimer, and AS_3 corresponds to trisolvated LiHMDS monomer.



A_2S_2 **AS_3**

Given $K_{eq} = [AS_3]^2/\{[A_2S_2][S]^4\}$, and $2[A_2S_2] + [AS_3] = [A]_0$, one can solve for $[A_2S_2]$ as a function of $[A]_0$ and $[S]$:

$$K_{eq} = \frac{[AS_3]^2}{[A_2S_2][S]^4} = \frac{([A]_0 - 2[A_2S_2])^2}{[A_2S_2][S]^4}$$

Rearranging,

$$4[A_2S_2]^2 - \left(4[A]_0 + K_{eq}[S]^4\right)[A_2S_2] + [A]_0^2 = 0$$

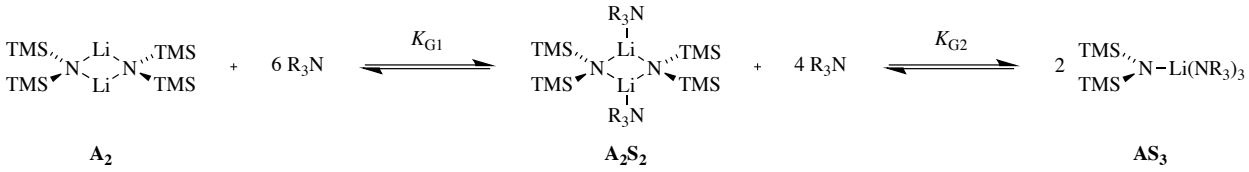
Applying the quadratic equation to $[A_2S_2]$ gives:

$$[A_2S_2] = \frac{\left(4[A]_0 + K_{eq}[S]^4\right) - \sqrt{\left(4[A]_0 + K_{eq}[S]^4\right)^2 - 16[A]_0^2}}{8} = \frac{4[A]_0 + K_{eq}[S]^4 - \sqrt{K_{eq}}[S]^2\sqrt{K_{eq}[S]^4 + 8[A]_0}}{8}$$

D.A.1.2. LiHMDS-mediated enolization: DMEA/hexane

To reduce complexity of the mathematical description of this mechanism, one must separate the equilibria describing the free base from that describing the ketone-solvated base. Under pseudo-first-order conditions, the total mass balance of the ketone-solvated base accounts for a small amount (5%) of the total base titer. By separating the mass balance equilibria, one can solve independently for the relevant species and then substitute them as needed.

To simplify the discussion of the mechanistic model, we introduce the following shorthand: A = a LiHMDS subunit, and S = R_3N. As shown below, A_2 corresponds to unsolvated LiHMDS dimer, A_2S_2 corresponds to disolvated LiHMDS dimer, and AS_3 corresponds to trisolvated LiHMDS monomer.



Given $K_{G1} = [A_2S_2]/\{[A_2][S]^2\}$, $K_{G2} = [AS_3]^2/\{[A_2S_2][S]^4\}$, and $2[A_2] + 2[A_2S_2] + [AS_3] = [A]_0$, one can solve for $[A_2S_2]$ as a function of $[A]_0$ and [S]:

$$\begin{aligned}[A]_0 &= 2[A_2] + 2[A_2S_2] + [AS_2T] + [AS_3] \\ &= 2\frac{[A_2S_2]}{K_{G1}[S]^2} + 2[A_2S_2] + \sqrt{K_{G2}[A_2S_2][S]^2[T]^2} + \sqrt{K_{G2}K_{G3}[A_2S_2][S]^4}\end{aligned}$$

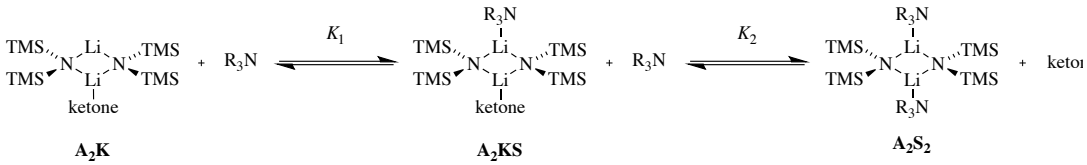
Rearranging to eliminate the square root affords a quadratic expression:

$$\left([A]_0 - \frac{2[A_2S_2]}{K_{G1}[S]^2} - 2[A_2S_2]\right)^2 = \left(\sqrt{K_{G2}[A_2S_2][S]^2[T]^2} + \sqrt{K_{G2}K3[A_2S_2][S]^4}\right)^2$$

This can be solved for $[A_2S_2]$ to provide:

$$[A_2S_2] = \frac{-4[A]_0 - \frac{4[A]_0}{K_{G1}[S]^2} - K_{G2}K_{G3}[S]^4 - 2K_{G2}\sqrt{K_{G3}}[S]^3[T] - K_{G2}[S]^2[T]^2 + \sqrt{4[A]_0^2\left(-4 - \frac{4}{K_{G1}[S]^2} - \frac{8}{K_{G1}[S]^2}\right) + \left(4[A]_0 + \frac{4[A]_0}{K_{G1}[S]^2} + K_{G2}K_{G3}[S]^4 + 2K_{G2}\sqrt{K_{G3}}[S]^3[T] + K_{G2}[S]^2[T]^2\right)^2}}{2\left(-4 - \frac{4}{K_{G1}[S]^2} - \frac{8}{K_{G1}[S]^2}\right)}$$

We now turn to the set of equilibria and mass balance equations that describe the ketone-solvated base. We introduce the following shorthand: A = a LiHMDS subunit, S = R_3N, and K = ketone. As shown below, A_2K corresponds to ketone-complexed LiHMDS dimer, A_2KS corresponds to amine-solvated, ketone-complexed LiHMDS dimer, and A_2S_2 corresponds to disolvated LiHMDS dimer.



Given $K_1 = [A_2KS]/\{[A_2K][S]\}$, $K_2 = \{[A_2S_2][K]\}/\{[A_2KS][S]\}$, and $[A_2K] + [A_2KS] + [K] = [K]_0$, one can solve for $[A_2KS]$ as a function of $[K]_0$, $[A_2S_2]$, and [S]:

$$[A_2KS] = \frac{K_1K_2[A_2S_2][K]_0[S]}{[A_2S_2] + K_1[A_2S_2][S] + K_1K_2[S]^2}$$

Substituting $[A_2S_2]$ into the equation for $[A_2SK]$ gives:

$$[A_2KS] = (k0\ k1\ kg1\ s\ (kg1\ kg2\ s\text{^}6 + 4\ a0\ (1 + kg1\ s\text{^}2) -$$
$$Sqrt[kg1]\ Sqrt[kg2]\ s\text{^}3\ Sqrt[8\ a0 + 8\ a0\ kg1\ s\text{^}2 + kg1\ kg2\ s\text{^}6]))/($$
$$kg1\ (kg1\ kg2\ s\text{^}6 + 4\ a0\ (1 + kg1\ s\text{^}2) -$$
$$Sqrt[kg1]\ Sqrt[kg2]\ s\text{^}3\ Sqrt[8\ a0 + 8\ a0\ kg1\ s\text{^}2 + kg1\ kg2\ s\text{^}6]) +$$
$$k1\ (8\ k2\ (1 + kg1\ s\text{^}2)\text{^}2 +$$
$$kg1\ s\ (4\ a0 + 4\ a0\ kg1\ s\text{^}2 + kg1\ kg2\ s\text{^}6 -$$
$$Sqrt[kg1]\ Sqrt[kg2]\ s\text{^}3\ Sqrt[8\ a0 +$$
$$8\ a0\ kg1\ s\text{^}2 + kg1\ kg2\ s\text{^}6])))$$

The form of the rate law is as follows:

$$\frac{d[P]}{dt} = k[A_2KS]$$

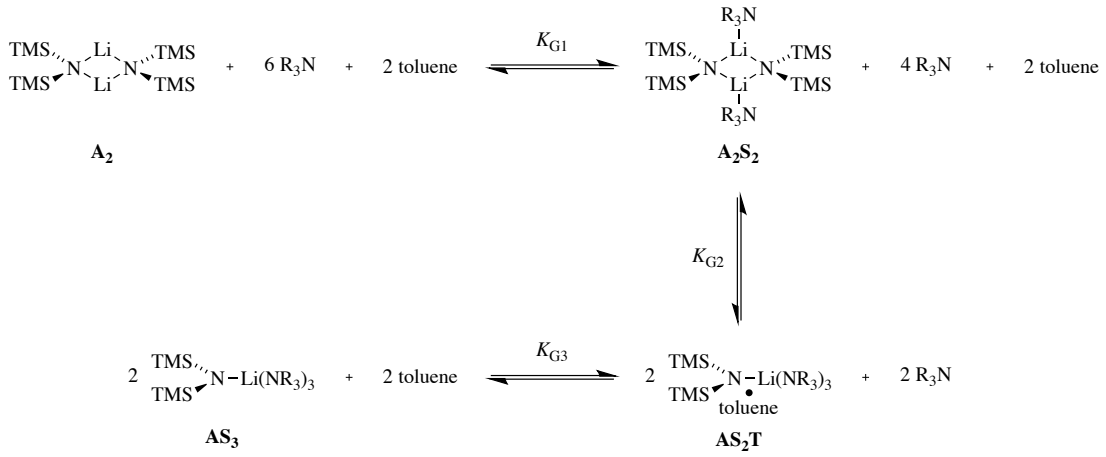
The fitting function to describe the enolization with LiHMDS in DMEA/hexane is found by inserting [A_2SK] into the rate law:

$$\frac{d[P]}{dt} = k(k0\ k1\ kg1\ s\ (kg1\ kg2\ s\text{^}6 + 4\ a0\ (1 + kg1\ s\text{^}2) -$$
$$Sqrt[kg1]\ Sqrt[kg2]\ s\text{^}3\ Sqrt[8\ a0 + 8\ a0\ kg1\ s\text{^}2 + kg1\ kg2\ s\text{^}6]))/($$
$$kg1\ (kg1\ kg2\ s\text{^}6 + 4\ a0\ (1 + kg1\ s\text{^}2) -$$
$$Sqrt[kg1]\ Sqrt[kg2]\ s\text{^}3\ Sqrt[8\ a0 + 8\ a0\ kg1\ s\text{^}2 + kg1\ kg2\ s\text{^}6]) +$$
$$k1\ (8\ k2\ (1 + kg1\ s\text{^}2)\text{^}2 +$$
$$kg1\ s\ (4\ a0 + 4\ a0\ kg1\ s\text{^}2 + kg1\ kg2\ s\text{^}6 -$$
$$Sqrt[kg1]\ Sqrt[kg2]\ s\text{^}3\ Sqrt[8\ a0 +$$
$$8\ a0\ kg1\ s\text{^}2 + kg1\ kg2\ s\text{^}6])))$$

D.A.1.3. LiHMDS-mediated enolization: DMEA/toluene

To reduce complexity of the mathematical description of this mechanism, one must separate the equilibria describing the free base from that describing the ketone-solvated base. Under pseudo-first-order conditions, the total mass balance of the ketone-solvated base accounts for a small amount (5%) of the total base titer. By separating the mass balance equilibria, one can solve independently for the relevant species and then substitute them as needed.

To simplify the discussion of the mechanistic model, we introduce the following shorthand: A = a LiHMDS subunit, S = R_3N, and T = toluene. As shown below, A_2 corresponds to unsolvated LiHMDS dimer, A_2S_2 corresponds to disolvated LiHMDS dimer, AS_2T corresponds to disolvated LiHMDS monomer with one bound toluene, and AS_3 corresponds to trisolvated LiHMDS monomer.



Given $K_{G1} = [A_2S_2]^2/\{[A_2][S]\}$, $K_{G2} = [AS_3]^2/\{[A_2S_2][S]^4\}$, $K_{G3} = [AS_2T]^2[S]^2/\{[AS_3][T]^2\}$, and $2[A_2] + 2[A_2S_2] + [AS_2T] + [AS_3] = [A]_0$, one can solve for $[A_2S_2]$ as a function of $[A]_0$ and [S]:

$$\begin{aligned}[\mathrm{A}]_0 &= 2[\mathrm{A}_2]+2[\mathrm{A}_2\mathrm{S}_2]+[\mathrm{AS}_3]+[\mathrm{AS}_2\mathrm{T}] \\ &= 2\frac{[\mathrm{A}_2\mathrm{S}_2]}{K_{\mathrm{G1}}[\mathrm{S}]^2}+2[\mathrm{A}_2\mathrm{S}_2]+\sqrt{K_{\mathrm{G2}}[\mathrm{A}_2\mathrm{S}_2][\mathrm{S}]^4}+\sqrt{K_{\mathrm{G2}}K_{\mathrm{G3}}[\mathrm{A}_2\mathrm{S}_2][\mathrm{S}]^2[\mathrm{T}]^2}\end{aligned}$$

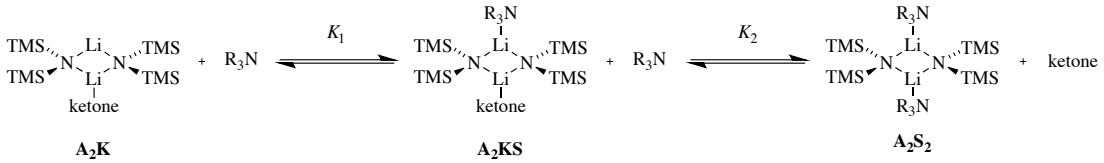
Rearranging to eliminate the square root affords a quadratic expression:

$$\left([\mathrm{A}]_0-2[\mathrm{A}_2\mathrm{S}_2]\left(1+\frac{1}{K_{\mathrm{G1}}[\mathrm{S}]^2}\right)\right)^2=\left(\sqrt{K_{\mathrm{G2}}[\mathrm{A}_2\mathrm{S}_2][\mathrm{S}]^4}+\sqrt{K_{\mathrm{G2}}K_{\mathrm{G3}}[\mathrm{A}_2\mathrm{S}_2][\mathrm{S}]^2[\mathrm{T}]^2}\right)^2$$

This can be solved for $[A_2S_2]$ to provide:

$$[\mathrm{A}_2\mathrm{S}_2]=\frac{\left(4[\mathrm{A}]_0\left(1+\frac{1}{K_{\mathrm{G1}}[\mathrm{S}]^2}\right)+K_{\mathrm{G2}}[\mathrm{S}]^4+K_{\mathrm{G2}}\sqrt{K_{\mathrm{G3}}}[\mathrm{S}]^3[\mathrm{T}]+K_{\mathrm{G2}}K_{\mathrm{G3}}[\mathrm{S}]^2[\mathrm{T}]^2-\sqrt{-16[\mathrm{A}]_0^2\left(1+\frac{1}{K_{\mathrm{G1}}[\mathrm{S}]^2}\right)^2+\left(-4[\mathrm{A}]_0\left(1+\frac{1}{K_{\mathrm{G1}}[\mathrm{S}]^2}\right)-K_{\mathrm{G2}}[\mathrm{S}]^4-K_{\mathrm{G2}}\sqrt{K_{\mathrm{G3}}}[\mathrm{S}]^3[\mathrm{T}]-K_{\mathrm{G2}}K_{\mathrm{G3}}[\mathrm{S}]^2[\mathrm{T}]^2\right)^2}\right)}{8\left(1+\frac{1}{K_{\mathrm{G1}}[\mathrm{S}]^2}\right)^2}$$

We now turn to the set of equilibria and mass balance equations that describe the ketone-solvated base. We introduce the following shorthand: A = a LiHMDS subunit, S = R_3N, and K = ketone. As shown below, A_2K corresponds to ketone-complexed LiHMDS dimer, A_2KS corresponds to amine-solvated, ketone-complexed LiHMDS dimer, and A_2S_2 corresponds to disolvated LiHMDS dimer.



A_2K **A_2KS** **A_2S_2**

Given $K_1 = [A_2KS]/\{[A_2K][S]\}$, $K_2 = \{[A_2S_2][K]\}/\{[\ A_2KS][S]\}$, and $[A_2K] + [A_2KS] + [K] = [K]_0$, one can solve for $[A_2KS]$ as a function of $[K]_0$, $[A_2S_2]$, and [S]:

$$[\mathrm{A}_2\mathrm{KS}]=\frac{K_1K_2[\mathrm{A}_2\mathrm{S}_2][\mathrm{K}]_0[\mathrm{S}]}{[\mathrm{A}_2\mathrm{S}_2]+K_1[\mathrm{A}_2\mathrm{S}_2][\mathrm{S}]+K_1K_2[\mathrm{S}]^2}$$

Substituting $[A_2S_2]$ into the equation for $[A_2SK]$ gives:

$$[A_2KS] = (k0\ k1\ s\ (4\ a0\ (1 + 1/(kg1\ s\text{^}2)) + kg2\ s\text{^}4 + kg2\ Sqrt[kg3]\ s\text{^}3\ t + kg2\ kg3\ s\text{^}2\ t\text{^}2 - Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 + (-4\ a0\ (1 + 1/(kg1\ s\text{^}2)) - kg2\ s\text{^}4 - kg2\ Sqrt[kg3]\ s\text{^}3\ t - kg2\ kg3\ s\text{^}2\ t\text{^}2)\text{^}2]))/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2\ (k1\ k2\ s\text{^}2 + (4\ a0\ (1 + 1/(kg1\ s\text{^}2)) + kg2\ s\text{^}4 + kg2\ Sqrt[kg3]\ s\text{^}3\ t + kg2\ kg3\ s\text{^}2\ t\text{^}2 - Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 + (-4\ a0\ (1 + 1/(kg1\ s\text{^}2)) - kg2\ s\text{^}4 - kg2\ Sqrt[kg3]\ s\text{^}3\ t - kg2\ kg3\ s\text{^}2\ t\text{^}2)\text{^}2])/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2) + (1/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2))k1\ s\ (4\ a0\ (1 + 1/(kg1\ s\text{^}2)) + kg2\ s\text{^}4 + kg2\ Sqrt[kg3]\ s\text{^}3\ t + kg2\ kg3\ s\text{^}2\ t\text{^}2 - Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 + (-4\ a0\ (1 + 1/(kg1\ s\text{^}2))\ -kg2\ s\text{^}4 - kg2\ Sqrt[kg3]\ s\text{^}3\ t - kg2\ kg3\ s\text{^}2\ t\text{^}2)\text{^}2])))$$

The form of the rate law is as follows:

$$\frac{d[P]}{dt} = k[A_2KS]$$

The fitting function to describe the enolization with LiHMDS in DMEA/toluene is found by inserting $[A_2SK]$ into the rate law:

$$\frac{d[P]}{dt} = k(k0\ k1\ s\ (4\ a0\ (1 + 1/(kg1\ s\text{^}2)) + kg2\ s\text{^}4 + kg2\ Sqrt[kg3]\ s\text{^}3\ t + kg2\ kg3\ s\text{^}2\ t\text{^}2 - Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 + (-4\ a0\ (1 + 1/(kg1\ s\text{^}2)) - kg2\ s\text{^}4 - kg2\ Sqrt[kg3]\ s\text{^}3\ t - kg2\ kg3\ s\text{^}2\ t\text{^}2)\text{^}2]))/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2\ (k1\ k2\ s\text{^}2 + (4\ a0\ (1 + 1/(kg1\ s\text{^}2)) + kg2\ s\text{^}4 + kg2\ Sqrt[kg3]\ s\text{^}3\ t + kg2\ kg3\ s\text{^}2\ t\text{^}2 - Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 + (-4\ a0\ (1 + 1/(kg1\ s\text{^}2)) - kg2\ s\text{^}4 - kg2\ Sqrt[kg3]\ s\text{^}3\ t - kg2\ kg3\ s\text{^}2\ t\text{^}2)\text{^}2])/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2) + (1/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2))k1\ s\ (4\ a0\ (1 + 1/(kg1\ s\text{^}2)) + kg2\ s\text{^}4 + kg2\ Sqrt[kg3]\ s\text{^}3\ t + kg2\ kg3\ s\text{^}2\ t\text{^}2 - Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 + (-4\ a0\ (1 + 1/(kg1\ s\text{^}2))\ -kg2\ s\text{^}4 - kg2\ Sqrt[kg3]\ s\text{^}3\ t - kg2\ kg3\ s\text{^}2\ t\text{^}2)\text{^}2])))$$

A more convenient form of the equation is found instead by writing the [T] as a function of [S] by replacing [T] with (9.41/9.23*(9.23–[S])):

$$\frac{d[P]}{dt} = k(k0\ k1\ s\ (4\ a0\ (1 + 1/(kg1\ s\text{^}2)) + 0.962109\ kg2\ kg3\ (9.41 - s)\text{^}2\ s\text{^}2 +$$
$$0.980871\ kg2\ Sqrt[kg3]\ (9.41 - s)\ s\text{^}3 + kg2\ s\text{^}4 - Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 +$$
$$(-4\ a0\ (1 + 1/(kg1\ s\text{^}2)) - 0.962109\ kg2\ kg3\ (9.41 - s)\text{^}2\ s\text{^}2 -$$
$$0.980871\ kg2\ Sqrt[kg3]\ (9.41 - s)\ s\text{^}3 - kg2\ s\text{^}4)\text{^}2]))/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2\ (k1\ k2\ s\text{^}2 +$$
$$1/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2)\ (4\ a0\ (1 + 1/(kg1\ s\text{^}2)) +$$
$$0.962109\ kg2\ kg3\ (9.41 - s)\text{^}2\ s\text{^}2 + 0.980871\ kg2\ Sqrt[kg3]\ (9.41 - s)\ s\text{^}3 + kg2\ s\text{^}4 -$$
$$Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 + (-4\ a0\ (1 + 1/(kg1\ s\text{^}2)) - 0.962109\ kg2\ kg3\ (9.41 - s)\text{^}2\ s\text{^}2$$
$$0.980871\ kg2\ Sqrt[kg3]\ (9.41 - s)\ s\text{^}3 - kg2\ s\text{^}4)\text{^}2]) + 1/(8\ (1 + 1/(kg1\ s\text{^}2))\text{^}2)k1\ s\ (4\ a0\ (1 +$$
$$1/(kg1\ s\text{^}2)) + 0.962109\ kg2\ kg3\ (9.41 - s)\text{^}2\ s\text{^}2 + 0.980871\ kg2\ Sqrt[kg3]\ (9.41 - s)\ s\text{^}3 +$$
$$kg2\ s\text{^}4 - Sqrt[-16\ a0\text{^}2\ (1 + 1/(kg1\ s\text{^}2))\text{^}2 + (-4\ a0\ (1 + 1/(kg1\ s\text{^}2)) -$$
$$0.962109\ kg2\ kg3\ (9.41 - s)\text{^}2\ s\text{^}2 - 0.980871\ kg2\ Sqrt[kg3]\ (9.41 - s)\ s\text{^}3 - kg2\ s\text{^}4)\text{^}2]))$$

IV: Ground State Computations

Chart A.1.1

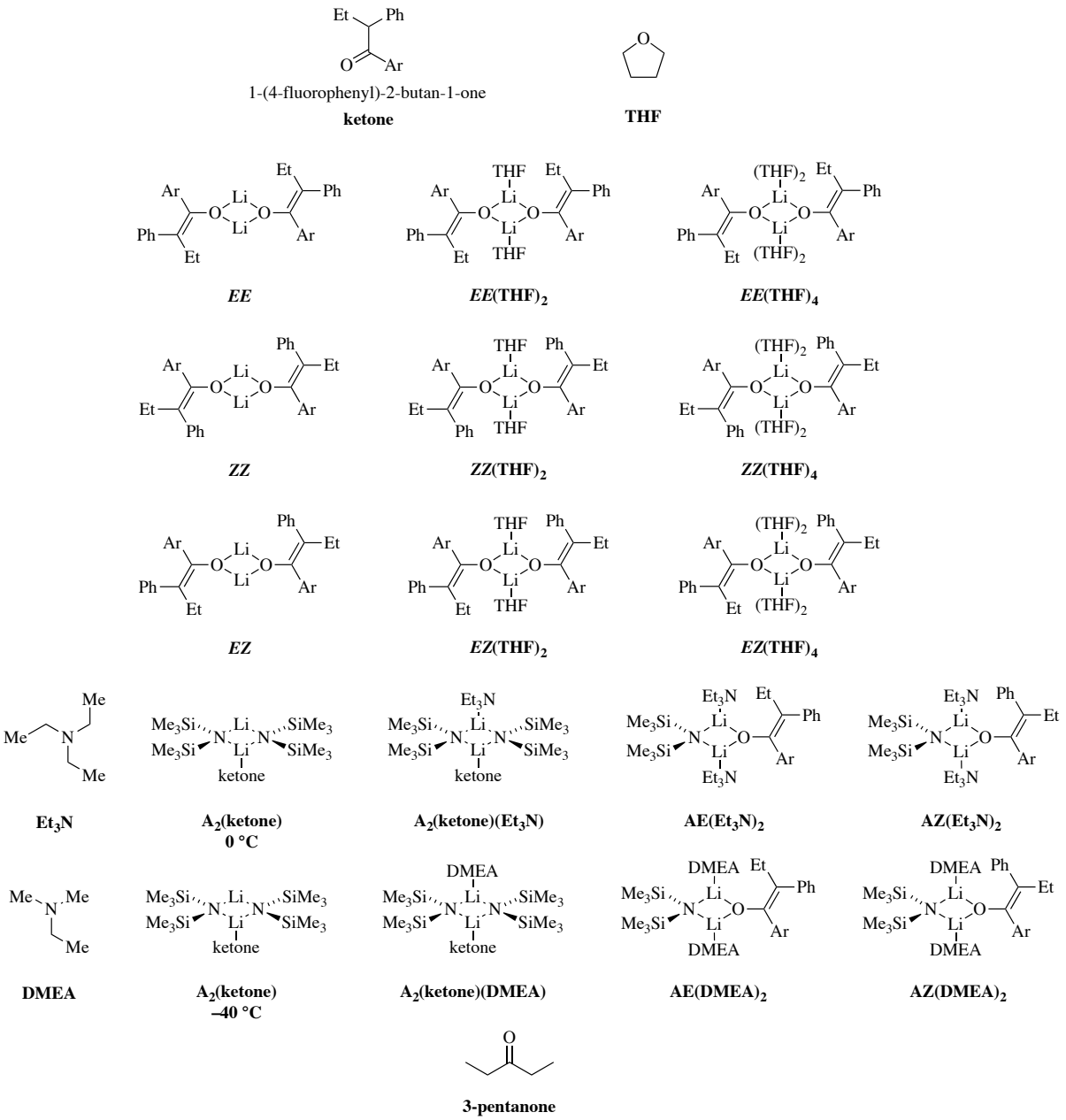
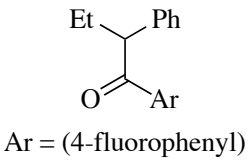
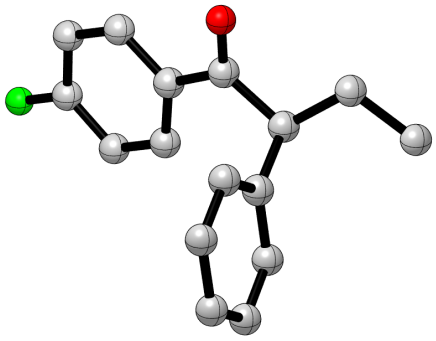


Table A.1.3. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant ground states of LiHMDS/THF-mediated enolizations at 0 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

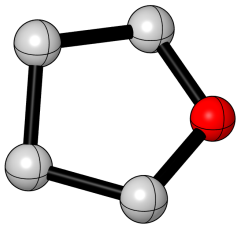


Ar = (4-fluorophenyl)



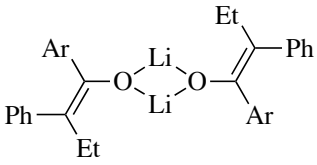
Ketone (1)
G = –793.561848
G_{MP2} = –496407.619

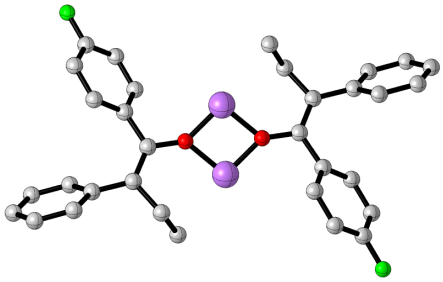
Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	-0.69956000	1.29593800	0.40874200
C	-1.06472200	1.52005500	1.74452100
C	-1.72657700	2.69092200	2.11420200
C	-2.03519200	3.65875100	1.15593600
C	-1.67809600	3.44610200	-0.17599600
C	-1.01414800	2.27437100	-0.54366100
H	-0.74545500	2.11317900	-1.58580100
H	-1.91583700	4.19085100	-0.93115700
H	-2.54967600	4.57107100	1.44537900
H	-1.99910000	2.84842200	3.15450200
H	-0.82157100	0.77454000	2.49679400
C	1.21371200	-0.24404000	0.91447900
C	2.51082100	0.45346900	0.63821000
C	2.67582400	1.41788500	-0.36888500
C	3.90984300	2.03039800	-0.57554600
C	4.98000900	1.66321000	0.23285900
C	4.85451100	0.71217900	1.24246800
C	3.61545700	0.11574100	1.43997800
H	3.47467700	-0.62614700	2.21877900
H	5.71692600	0.45822700	1.85002500
F	6.17620400	2.24786100	0.03386400
H	4.05224500	2.78203600	-1.34475800
H	1.83743800	1.71657700	-0.98790100
O	1.11562300	-0.99808300	1.87334500
C	-0.94612900	-1.22274700	0.03147200
C	-2.10407200	-1.12315700	-0.96483000
H	-2.74018100	-0.25574800	-0.75917600
H	-1.73996000	-1.03255500	-1.99636700
H	-2.73267800	-2.01920400	-0.91470300
H	-0.35224600	-2.12084300	-0.17913300
H	-1.32853300	-1.34712600	1.04950100
H	0.35899400	0.12334600	-1.02944000



THF
G = –232.357946
G_{MP2} = –145317.706

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
H	0.36944100	0.05245400	1.03607400
H	0.78366900	0.39304900	-0.65835500
C	-0.43145400	-1.42747100	-0.35907500
H	-0.36819400	-1.58569300	-1.44243900
H	0.17898100	-2.19202000	0.13156300
C	-1.89873200	-1.42780000	0.09478400
H	-2.50889400	-2.19240900	-0.39610500
H	-1.96191900	-1.58645800	1.17808700
C	-2.33082600	-0.00036200	-0.26378100
H	-2.70107000	0.05220800	-1.29954200
H	-3.11413200	0.39228800	0.39526100
O	-1.16547600	0.82075200	-0.13234900

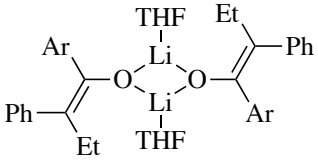


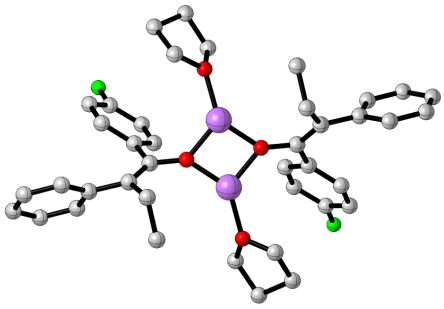


EE
G = –1601.154102
G_{MP2} = –1001565.934

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	0.93246200	-1.19198700	0.13901900
C	2.38807600	-0.91363300	0.23310500
C	3.17334200	-1.43586700	1.27908300
C	4.53466300	-1.15162300	1.37608700
C	5.15169600	-0.32176000	0.43782300
C	4.38908000	0.21819300	-0.59960300
C	3.02913100	-0.07306200	-0.69850000
H	2.45650600	0.34294300	-1.52418500
H	4.85538200	0.86438100	-1.33945900
H	6.21141800	-0.09433800	0.51704500
H	5.11268900	-1.57022900	2.19638700
H	2.70051400	-2.06682700	2.02583600
C	0.37074200	-2.43470100	0.25018500
C	1.12853500	-3.72445600	0.25670700
C	2.17424700	-3.98834100	-0.64312700
C	2.80972900	-5.22869100	-0.66748500
C	2.39280100	-6.21458100	0.21989400
C	1.35975800	-5.99722600	1.12425500
C	0.72981200	-4.75267400	1.12910300
H	-0.06971900	-4.56056200	1.84011000
H	1.06907700	-6.78823000	1.80835300
F	3.00558800	-7.41813200	0.20093100
H	3.61338800	-5.44127100	-1.36509700
H	2.48924800	-3.21420000	-1.33454500
O	-0.95361500	-2.58992900	0.31697100
Li	-2.31292200	-1.39219300	0.54911500
O	-3.64727200	-2.55923100	0.22001300
C	-4.97157300	-2.71422900	0.28909900
C	-5.53326100	-3.95677700	0.40198000
C	-6.98910000	-4.23497500	0.31039000
C	-7.62887200	-5.07447500	1.24384700

C	-8.98901700	-5.36557700	1.14733300
C	-9.75312300	-4.82653300	0.11051500
C	-9.13738500	-3.99774100	-0.82952800
C	-7.77585100	-3.71365600	-0.73489900
H	-7.30405500	-3.08352700	-1.48300700
H	-9.71659200	-3.57985100	-1.64936000
H	-10.8130080	-5.05383700	0.03316100
H	-9.45432600	-6.01091900	1.88855100
H	-7.05503200	-5.48975300	2.06905600
C	-4.60081300	-5.14886000	0.54025700
C	-4.04240600	-5.66397200	-0.80557200
H	-4.85842300	-6.03003700	-1.43709800
H	-3.55510400	-4.87036000	-1.39345700
H	-3.33040900	-6.48898500	-0.66726900
H	-3.77331800	-4.89834200	1.22700400
H	-5.12448600	-5.98391100	1.01773000
C	-5.72917200	-1.42436900	0.28282400
C	-6.77371300	-1.15974700	1.18379200
C	-7.40896600	0.08072900	1.20817300
C	-6.99297300	1.06600100	0.31968300
C	-5.96106300	0.84792100	-0.58580900
C	-5.33133200	-0.39672800	-0.59068300
H	-4.53264900	-0.58940200	-1.30248200
H	-5.67107700	1.63847500	-1.27072400
F	-7.60554200	2.26966200	0.33864300
H	-8.21172500	0.29385100	1.90665600
H	-7.08799500	-1.93338900	1.87609400
Li	-2.28805300	-3.75703000	-0.01179800
C	-0.56023200	0.51447500	1.34533900
H	-1.04788600	-0.27948400	1.93247500
H	0.25489800	0.88065800	1.97793800
H	-1.27238600	1.33925800	1.20646600
H	0.52415000	0.83537100	-0.47639100
H	-0.82651900	-0.25038500	-0.68795000

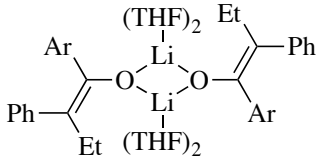


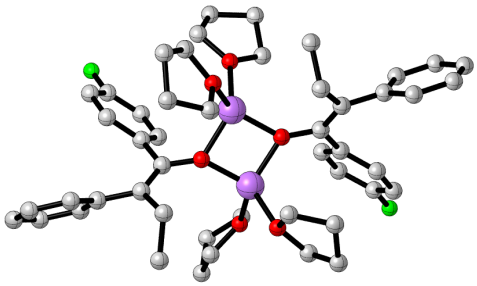


***EE*(THF)$_2$**
G = –2065.891771
G_{MP2} = –1292228.293

Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
O	1.49717000	1.06038300	0.00711400
C	2.82133100	0.98789400	0.16275300
C	3.63268700	0.32649000	-0.72091200
C	3.03587200	-0.25361600	-1.99103100
C	2.75043900	-1.76547600	-1.91029500
H	3.65930700	-2.32252800	-1.65536200
H	1.99679100	-1.98047500	-1.14363800
H	2.37774400	-2.14908400	-2.86914800
H	2.10814000	0.27821300	-2.22839500
H	3.72260200	-0.08187200	-2.83111000
C	5.07344400	0.04885800	-0.47904900
C	5.52080300	-0.53835600	0.72109600
C	6.86842400	-0.82426700	0.93458200
C	7.81414200	-0.54816900	-0.05503600
C	7.39178000	0.01715500	-1.25989500
C	6.04363800	0.30735100	-1.46788800
H	5.73745000	0.75859100	-2.40842700
H	8.11552400	0.23729200	-2.04129500
H	8.86418000	-0.77709900	0.10726900
H	7.17907000	-1.27691200	1.87338100
H	4.79186200	-0.77424700	1.49109000
C	3.32450600	1.75022700	1.35578900
C	2.56162500	1.76576000	2.53725900
C	2.95236200	2.50626800	3.65355900
C	4.11748200	3.26030700	3.57744000
C	4.89270700	3.29054300	2.42346300
C	4.49000800	2.53610200	1.32125300
H	5.09193100	2.55512500	0.41939900
H	5.79365800	3.89558700	2.39812500
F	4.50244900	3.98910000	4.64982100
H	2.37491300	2.50175300	4.57299300

H	1.64879800	1.17890900	2.57862200
Li	0.26770600	2.44881900	0.00108000
O	-1.22942300	1.38832700	0.00642800
C	-2.55351800	1.46205300	0.16215100
C	-3.36427700	2.12457000	-0.72121500
C	-4.80481000	2.40332900	-0.47923800
C	-5.77520500	2.14601600	-1.46818800
C	-7.12310500	2.43724500	-1.26009300
C	-7.54500800	3.00245600	-0.05501500
C	-6.59907800	3.27738200	0.93471800
C	-5.25168600	2.99043700	0.72113000
H	-4.52256700	3.22539200	1.49124100
H	-6.90935300	3.72991200	1.87369600
H	-8.59486100	3.23218800	0.10736000
H	-7.84703400	2.21801100	-2.04157500
H	-5.46937600	1.69488500	-2.40889600
C	-2.76702600	2.70459200	-1.99116600
C	-2.48100800	4.21633900	-1.91026500
H	-3.38968700	4.77372600	-1.65539700
H	-1.72736300	4.43097100	-1.14350300
H	-2.10805900	4.59986600	-2.86905100
H	-1.83948400	2.17239800	-2.22843600
H	-3.45369100	2.53320500	-2.83137800
C	-3.05738300	0.69975400	1.35491100
C	-4.22351100	-0.08515500	1.32004100
C	-4.62693800	-0.83957200	2.42201000
C	-3.85180400	-0.81028500	3.57606600
C	-2.68606400	-0.05722700	3.65250500
C	-2.29461400	0.68326200	2.53645000
H	-1.38130300	1.26934100	2.57805900
H	-2.10869900	-0.05345300	4.57199600
F	-4.23747000	-1.53904800	4.64821600
H	-5.52837700	-1.44387700	2.39640900
H	-4.82535600	-0.10344000	0.41812100
O	0.70573000	4.32313800	0.11010900
C	1.80373400	4.85607800	-0.67844700
H	1.38535100	5.28468500	-1.59724900
H	2.46887900	4.02784200	-0.93810400
C	2.46276100	5.91782000	0.20235900
H	3.21757900	5.45685100	0.84853100
H	2.94505100	6.70304700	-0.38707900
C	1.27825800	6.42774100	1.03847600
H	1.58498600	6.91164600	1.97010900
H	0.67758100	7.14126600	0.46252300
C	0.48868700	5.14277200	1.28785400
H	0.86766200	4.60150200	2.16335900
H	-0.58849600	5.29711500	1.39504700
O	-0.43818000	-1.87445200	0.10837800
C	-1.53713900	-2.40675800	-0.67931400
H	-1.11960900	-2.83651900	-1.59796100
H	-2.20145600	-1.57796900	-0.93934700
C	-2.19697800	-3.46709800	0.20256500
H	-2.95100000	-3.00480300	0.84871800
H	-2.68040600	-4.25222300	-0.38607900
C	-1.01268800	-3.97772500	1.03855300
H	-1.31956600	-4.46062100	1.97066000
H	-0.41303700	-4.69232400	0.46286200
C	-0.22160600	-2.69345300	1.28667800
H	-0.59969200	-2.15112100	2.16191500
H	0.85544400	-2.84887700	1.39359100



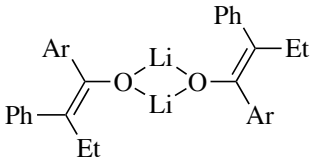


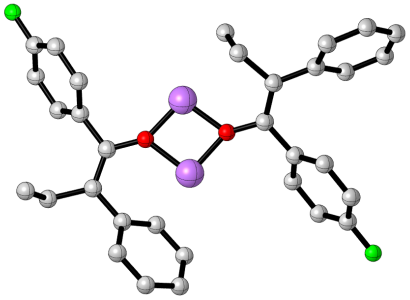
***EE*(THF)$_4$**
G = –2530.594829
G_{MP2} = –1582879.312

Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
O	-1.53108300	-1.15644100	0.07719600
C	-2.85589300	-1.09899400	0.06426400
C	-3.58288400	-0.26058200	-0.75185200

C	-2.87448800	0.57612700	-1.80189500
C	-2.77349700	2.07294700	-1.45591900
H	-3.76624300	2.50450600	-1.28414700
H	-2.17601100	2.22192700	-0.54991000
H	-2.29645100	2.63544800	-2.26894800
H	-1.86824800	0.17818500	-1.95592400
H	-3.39819000	0.48545200	-2.76492500
C	-5.05066200	-0.05006400	-0.63203600
C	-5.66767500	0.22577500	0.60545700
C	-7.03960600	0.44962700	0.70631600
C	-7.84580500	0.42684000	-0.43369100
C	-7.25617900	0.17636900	-1.67410800
C	-5.88422000	-0.05489000	-1.76959700
H	-5.45097700	-0.26023800	-2.74531400
H	-7.86769500	0.15583500	-2.57347600
H	-8.91464100	0.60896200	-0.35764100
H	-7.47883900	0.65676800	1.67955000
H	-5.05235800	0.26401700	1.49963200
C	-3.52302200	-2.07571000	0.99848500
C	-3.00685600	-2.26591700	2.29036000
C	-3.57573000	-3.17635800	3.18151000
C	-4.66205500	-3.93236000	2.75826100
C	-5.18951500	-3.79814600	1.47937600
C	-4.61752200	-2.86875800	0.61082200
H	-5.03470000	-2.74872000	-0.38332400
H	-6.03402500	-4.41105300	1.18035000
F	-5.21542700	-4.82593100	3.61052100
H	-3.19338800	-3.30566000	4.18954500
H	-2.14708800	-1.67994400	2.59790000
Li	-0.27850900	-2.61292400	0.01844900
O	1.23172600	-1.47762600	-0.12483800
C	2.55292500	-1.49639900	-0.03822500
C	3.38240500	-2.08581800	-0.96715100
C	4.85563600	-2.20375100	-0.80891800
C	5.72423100	-1.89551500	-1.87685600
C	7.10722000	-2.03363900	-1.76058000
C	7.67396800	-2.49132400	-0.56977100
C	6.83381900	-2.81781700	0.49711800
C	5.45191800	-2.68691700	0.37393100
H	4.81298500	-2.96403600	1.20717100
H	7.25585600	-3.19126000	1.42744400
H	8.75137700	-2.60096000	-0.47773100
H	7.74473000	-1.77896800	-2.60436300
H	5.30733400	-1.53129200	-2.81262800
C	2.79000600	-2.66884900	-2.24113600
C	3.14646400	-4.14017700	-2.51500400
H	4.22864600	-4.28342600	-2.60235700
H	2.79094600	-4.78865500	-1.70641300
H	2.68581400	-4.48518100	-3.44949200
H	1.70315400	-2.56986800	-2.18521600
H	3.10874700	-2.07676100	-3.11560900
C	3.08378400	-0.76322500	1.16749500
C	4.12280100	0.17930800	1.08992600
C	4.55851500	0.87723800	2.21776800
C	3.94764900	0.62279900	3.44001900
C	2.90538300	-0.29019200	3.55973800
C	2.47194400	-0.96238300	2.41667700
H	1.64319400	-1.65996400	2.48257100
H	2.45102600	-0.46061500	4.53116100
F	4.37114400	1.28624600	4.54102100
H	5.36235600	1.60449900	2.16087200
H	4.60655000	0.35962000	0.13573000
O	0.17419200	-4.13137000	1.34502300
C	-0.00703500	-4.19940100	2.77656500
H	-0.91474700	-4.77700900	2.98860100
H	-0.15101500	-3.18248900	3.15380300
C	1.24663900	-4.88335800	3.32757600
H	2.03693800	-4.14604400	3.51117500
H	1.05307800	-5.41632700	4.26339200
C	1.64149300	-5.80826400	2.16660300
H	2.69360400	-6.10692600	2.18860200
H	1.02768700	-6.71698700	2.17609100
C	1.30811300	-4.94481000	0.94938600
H	2.13547200	-4.27994400	0.67744200
H	1.01755900	-5.52145400	0.06699200
O	-0.89453400	-3.84985600	-1.48608200
C	-1.23083500	-3.21455400	-2.74183400
H	-0.50560600	-3.53437200	-3.50215700
H	-1.15240600	-2.13436000	-2.60015900
C	-2.64676600	-3.68321900	-3.07611600
H	-3.37859700	-3.04339100	-2.57128400
H	-2.85208100	-3.66346100	-4.15082700
C	-2.65960300	-5.09900400	-2.47977600
H	-3.66637700	-5.47205200	-2.26950500
H	-2.17007900	-5.80515400	-3.16114700
C	-1.83257300	-4.91798800	-1.20408400
H	-2.45856800	-4.61533100	-0.35785000
H	-1.26416000	-5.81017400	-0.92436400
O	0.59299700	1.21909900	-1.57454700
C	0.87112900	0.57869200	-2.83822000
H	0.06222000	0.81309700	-3.54493200
H	0.89898800	-0.49643500	-2.65866300

C	2.20256200	1.16426600	-3.29992200
H	3.02908600	0.64868200	-2.79821300
H	2.34747000	1.08440700	-4.38165200
C	2.08568700	2.61537800	-2.80826000
H	3.05273400	3.11177500	-2.68389600
H	1.48965000	3.20867300	-3.51155100
C	1.34287100	2.45074800	-1.47506000
H	2.04125000	2.35810600	-0.63563700
H	0.64679500	3.27011900	-1.26733700
O	-0.23754000	1.38913700	1.49067500
C	-1.40716400	1.29607600	2.33707100
H	-1.31640700	0.40286700	2.96819700
H	-2.28179400	1.18304800	1.69320200
C	-1.39754800	2.56782300	3.18269800
H	-1.84809700	3.40026400	2.62895700
H	-1.94356100	2.44867600	4.12339500
C	0.10889900	2.79974600	3.37476200
H	0.36320000	3.83140900	3.63568400
H	0.50034200	2.14412000	4.16123200
C	0.67090000	2.38869200	2.01150900
H	0.68556900	3.23742500	1.31643500
H	1.67143700	1.95336600	2.06554300

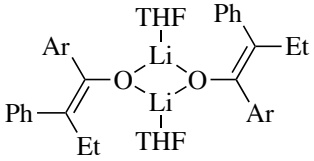


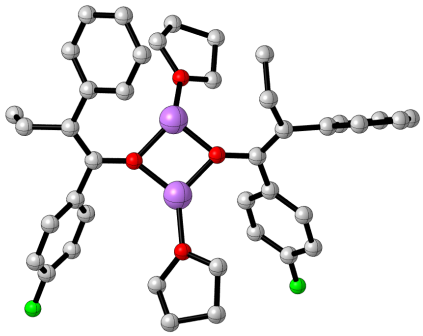


EZ
G = –1601.159815
G_{MP2} = –1001571.168

Atom	**X**	**Y**	**Z**
C	0.00000000	0.00000000	0.00000000
C	-1.09460600	1.01297500	-0.29121400
C	-2.49690100	0.52439500	-0.26143700
C	-2.98795300	-0.21061900	0.83581600
C	-4.29289600	-0.70141400	0.85744200
C	-5.14938700	-0.47321000	-0.22135900
C	-4.68098500	0.24708000	-1.32203100
C	-3.37360700	0.73041900	-1.34428800
H	-3.01501300	1.27374300	-2.21345500
H	-5.33243600	0.42351300	-2.17455800
H	-6.16646600	-0.85582000	-0.20642200
H	-4.64337200	-1.25816200	1.72327300
H	-2.34242000	-0.38283900	1.69397900
C	-0.71925000	2.28117800	-0.64660900
C	-1.66328300	3.42599500	-0.83773200
C	-2.70954900	3.69485600	0.05978500
C	-3.53450000	4.80617100	-0.10529100
C	-3.30812700	5.65485500	-1.18278000
C	-2.28070100	5.42841100	-2.09132100
C	-1.45847400	4.31769100	-1.90459300
H	-0.65190000	4.12225700	-2.60557900
H	-2.14010800	6.11081600	-2.92372500
F	-4.10572400	6.73301300	-1.34968300
H	-4.34030300	5.02372900	0.58831900
H	-2.87596300	3.02720600	0.89836000
O	0.56566100	2.60148500	-0.81357200
Li	1.80934900	3.90935800	-0.57316100
O	3.27211900	2.75356800	-0.71948900
Li	2.01679000	1.49750900	-0.92940200
C	4.56925900	3.04766800	-0.69678500
C	5.05090100	4.31682800	-0.51192900
C	4.09291800	5.44868500	-0.45273200
C	4.12508500	6.40687300	0.58057800
C	3.21397000	7.46386200	0.62746800
C	2.23376600	7.60647400	-0.35626000
C	2.19479800	6.68727300	-1.40911300
C	3.11454400	5.63494400	-1.45986700
H	3.11545800	4.96194700	-2.31574300
H	1.46575200	6.80284700	-2.20757500
H	1.52413800	8.42758600	-0.31537600
H	3.26748500	8.17803000	1.44545900
H	4.86867600	6.31634300	1.36639700
C	6.51998800	4.61713600	-0.22962300
C	6.99137400	4.26774800	1.19541100

H	6.41526200	4.80283100	1.95904900
H	8.04909300	4.52583100	1.33186200
H	6.87744000	3.19592700	1.38966500
H	7.16298000	4.08273900	-0.93724200
H	6.70191400	5.68303700	-0.41521400
C	5.45704800	1.84742200	-0.84307300
C	6.37335500	1.73103700	-1.89890300
C	7.13558400	0.57474200	-2.07169400
C	6.97372600	-0.47213900	-1.17253200
C	6.07275000	-0.39969000	-0.11515700
C	5.31422800	0.76062000	0.03657900
H	4.61184400	0.83673500	0.86298800
H	5.98168900	-1.23638300	0.57021100
F	7.70891900	-1.59369200	-1.33059800
H	7.84027300	0.47377300	-2.89083700
H	6.47793500	2.55069500	-2.60381200
C	0.56773600	-0.68438800	-1.26529300
H	-0.21426100	-1.27308100	-1.75553600
H	0.90161000	0.03788200	-2.02729100
H	1.40002500	-1.36229000	-1.03141600
H	0.80985000	0.47929900	0.57739700
H	-0.38106300	-0.79208800	0.65347800





***EZ*(THF)$_2$**
G = –2065.892276
G_{MP2} = –1292230.824

Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
O	1.27530900	1.27387100	-0.47021700
C	2.58780200	1.47692400	-0.36303700
C	3.52059400	0.64986700	-0.93660300
C	3.06165100	-0.46732700	-1.85791000
C	3.13490700	-1.87256700	-1.23252100
H	4.15004700	-2.09522000	-0.88405900
H	2.45685700	-1.95342200	-0.37508700
H	2.85129400	-2.64512700	-1.95862500
H	2.03463200	-0.26386600	-2.17764500
H	3.67676800	-0.46937400	-2.76875600
C	4.98151100	0.73837800	-0.67461900
C	5.49711800	0.82188300	0.63478200
C	6.86798000	0.87915400	0.87904700
C	7.77666000	0.83494500	-0.18039700
C	7.29130600	0.73310200	-1.48540300
C	5.91856200	0.68312200	-1.72651600
H	5.56524600	0.61743200	-2.75226600
H	7.98452900	0.69671900	-2.32268500
H	8.84633900	0.87171800	0.00851200
H	7.22819900	0.94504300	1.90312700

Atom	X	Y	Z
H	4.80328700	0.84129600	1.47029900
C	2.93687400	2.73350600	0.38599000
C	2.17828100	3.10207300	1.51152300
C	2.41976200	4.29066100	2.20114600
C	3.42236600	5.13549900	1.74008300
C	4.18263400	4.82239200	0.61894000
C	3.93457800	3.62380600	-0.04965500
H	4.52583100	3.37315100	-0.92370100
H	4.95065400	5.51160300	0.28225400
F	3.65938900	6.29508700	2.39463300
H	1.84753600	4.56665800	3.08153100
H	1.39044900	2.43767600	1.85497100
Li	-0.16282900	2.42190700	-0.68583700
O	-0.22870500	4.18356900	-1.45056500
C	0.81884900	4.70858600	-2.30860600
H	0.70411300	4.25544500	-3.30101700
H	1.78410500	4.41418500	-1.88961400
C	0.60050300	6.22283200	-2.34468000
H	1.14128500	6.70611500	-1.52300100
H	0.94174300	6.66766400	-3.28396000
C	-0.91699400	6.34155800	-2.13075800

H	-1.22593700	7.32186700	-1.75654400
H	-1.45433100	6.14755600	-3.06664900
C	-1.18225100	5.22587500	-1.12183000
H	-0.99549900	5.56108100	-0.09384900
H	-2.18436700	4.79580800	-1.17793600
O	-1.45338700	1.18044200	-0.25048900
C	-2.76507400	1.01357400	-0.23396600
C	-3.41490600	-0.17110800	-0.50007000
C	-4.89779600	-0.34357400	-0.18375900
C	-5.20023200	-0.65460100	1.29586400
H	-4.67703300	-1.55443800	1.63946200
H	-6.27514300	-0.80758500	1.45728300
H	-4.87773000	0.17548600	1.93437700
H	-5.45627100	0.55739500	-0.45246600
H	-5.31139500	-1.14135700	-0.81301600
C	-2.67899500	-1.35917600	-0.98225900
C	-3.11926900	-2.67154900	-0.69353900
C	-2.44722200	-3.79780200	-1.16895800
C	-1.30506900	-3.66699300	-1.96060600
C	-0.86174900	-2.38173200	-2.28580800
C	-1.53359000	-1.25528400	-1.81142900
H	-1.20276900	-0.27105600	-2.12632700
H	0.00340800	-2.25132000	-2.93199900
H	-0.78385500	-4.54443500	-2.33363500
H	-2.82391700	-4.78690900	-0.91756700
H	-4.00410900	-2.81802900	-0.08292000
C	-3.50827500	2.26463000	0.15225400
C	-4.42765300	2.87762400	-0.71329400
C	-5.04750000	4.08390700	-0.37870500
C	-4.73783100	4.67706400	0.83944800
C	-3.82457600	4.10844400	1.72114000
C	-3.20877000	2.90911800	1.36417600
H	-2.48507500	2.45605400	2.03605200
H	-3.61096600	4.60271100	2.66372300
F	-5.33464300	5.84331900	1.17365300
H	-5.75812200	4.56393800	-1.04418200
H	-4.65313700	2.40712900	-1.66621000
O	0.44497600	-1.23744400	1.42385000
C	-0.18016500	-2.51269800	1.72716300
H	0.04281100	-3.20500600	0.90823300
H	-1.26122900	-2.36147700	1.76864300
C	0.43767000	-2.96648800	3.05130300
H	-0.13091900	-2.56626100	3.89906300
H	0.46273600	-4.05617400	3.14416900
C	1.83503800	-2.32817600	2.99666200
H	2.30007600	-2.21626500	3.98051600
H	2.50556600	-2.92392400	2.36655400
C	1.54245600	-0.98272400	2.33447000
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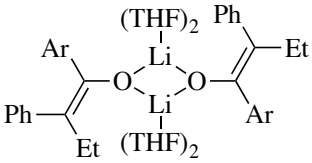
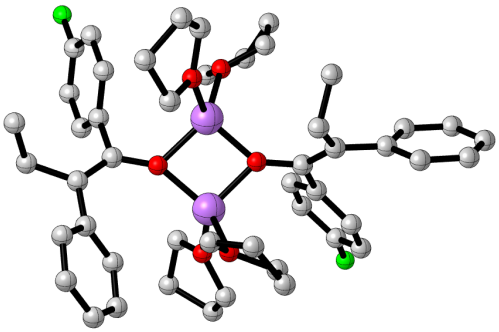


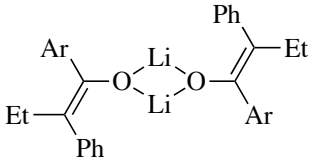


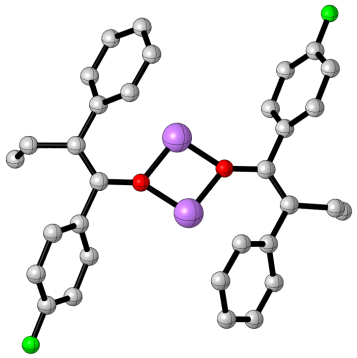
***EZ*(THF)$_4$**
G = –2530.587136
G_{MP2} = –1582876.586

Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
O	1.55876700	1.03256500	0.24687600
C	2.87883000	0.96628500	0.20096100
C	3.59985500	0.80447500	-0.96302700
C	2.87556800	0.82611800	-2.29877800
C	3.01555700	-0.46818400	-3.11894200
H	4.06476400	-0.68484500	-3.34707100
H	2.61770200	-1.32624000	-2.56413500
H	2.47361500	-0.39586900	-4.07122200
H	1.81756700	1.02854900	-2.11253200
H	3.24814300	1.65845400	-2.91882200
C	5.06625800	0.56973600	-1.01293300
C	5.70194400	-0.39146900	-0.19978600
C	7.07343500	-0.62505100	-0.27752400
C	7.86119200	0.07983800	-1.19062600
C	7.25270100	1.02048000	-2.02331700

C	5.88109300	1.25787900	-1.93637100
H	5.43249200	2.00238700	-2.58917400
H	7.84893400	1.57684200	-2.74317400
H	8.92963300	-0.10773500	-1.25805800
H	7.52730800	-1.37291900	0.36882500
H	5.10132300	-0.96181300	0.50270600
C	3.54171000	1.14849400	1.54374600
C	2.97423000	0.54368800	2.67713200
C	3.51926500	0.71240400	3.95004400
C	4.63218800	1.53295800	4.09382000
C	5.20777100	2.17796800	3.00579100
C	4.65928500	1.97814600	1.73817600
H	5.11164500	2.47166500	0.88496300
H	6.06921700	2.82089400	3.15684000
F	5.15794500	1.71911500	5.32742700
H	3.09490700	0.22693900	4.82391100
H	2.08323500	-0.06114700	2.54851700
Li	0.36831200	2.41191800	0.86527700
O	0.52567900	3.03353800	2.79432100
C	1.36785400	4.08213900	3.32623700
H	1.00886300	5.03428500	2.91848100
H	2.39566400	3.91530200	2.98960000
C	1.22711100	4.01485700	4.85534500
H	2.03990700	3.41961800	5.28516100
H	1.25297600	5.00578700	5.31833600
C	-0.11803900	3.29300600	5.04193200
H	-0.20669500	2.79167900	6.01061800
H	-0.95381400	3.99540200	4.94071300
C	-0.10460700	2.31329800	3.87099800
H	0.48850900	1.41919100	4.10629300
H	-1.09066200	2.00200000	3.52102400
O	0.90052800	4.06167300	-0.25509700
C	0.18529900	4.31739700	-1.49145200
H	-0.52350800	5.13212000	-1.31588400
H	-0.37756700	3.41742600	-1.74917800
C	1.25244900	4.69286100	-2.52194100
H	1.65608400	3.79581500	-3.00571900
H	0.86223600	5.35657500	-3.29976100
C	2.32850100	5.34843300	-1.64365500
H	3.32004700	5.36153300	-2.10636400
H	2.04885200	6.38092700	-1.40206200
C	2.28142400	4.47021600	-0.39271200
H	2.90523300	3.57632700	-0.50684800
H	2.57223100	4.99598500	0.52184100
O	-1.21227300	1.32400900	0.74369200
C	-2.52461500	1.20793000	0.86368600
C	-3.47577700	2.16758500	0.60303900
C	-4.96612400	1.81900500	0.60588500
C	-5.50793200	1.19269100	-0.69471500
H	-5.33512700	1.83774100	-1.56406400
H	-6.58866400	1.01271900	-0.62292000
H	-5.02207200	0.23130300	-0.89561600
H	-5.19354000	1.12834900	1.42544300
H	-5.53855000	2.73049800	0.81919800
C	-3.14722700	3.58981300	0.33483300
C	-3.85762500	4.34303500	-0.62503800
C	-3.64805800	5.71228500	-0.78940200
C	-2.71999200	6.38680700	0.00636900
C	-2.00244300	5.66238300	0.96160600
C	-2.20920100	4.29246400	1.11864400
H	-1.65341300	3.75969200	1.88132600
H	-1.28170600	6.16940600	1.59959300
H	-2.56544100	7.45664300	-0.10927800
H	-4.21946500	6.25493600	-1.53941800
H	-4.59502400	3.84948900	-1.25092300
C	-2.97916600	-0.15680200	1.34395500
C	-3.33353300	-0.34341600	2.68977300
C	-3.74184400	-1.58790700	3.17288000
C	-3.80054300	-2.65790400	2.28749800
C	-3.45265800	-2.51944300	0.94934400
C	-3.03568200	-1.26766800	0.48995400
H	-2.74631700	-1.15082900	-0.54904500
H	-3.51596100	-3.37803500	0.28780100
F	-4.21007200	-3.86577900	2.74025400
H	-4.02458900	-1.73366600	4.21078900
H	-3.30865900	0.50815800	3.36504200
O	-0.74515900	-0.33937900	-1.90846900
C	-1.39467100	0.74442300	-2.60993900
H	-0.63026000	1.36797000	-3.09509600
H	-1.92902900	1.34070200	-1.86795500
C	-2.28799700	0.06373800	-3.64360800
H	-3.22634500	-0.26108800	-3.17884700
H	-2.53406400	0.71961000	-4.48412500
C	-1.42962800	-1.14518900	-4.05046700
H	-2.01308700	-1.97244500	-4.46537500
H	-0.68856500	-0.84719100	-4.80103400
C	-0.73441700	-1.52566200	-2.73345900
H	-1.27297800	-2.31480000	-2.19488300
H	0.30110100	-1.84650100	-2.88131300
O	0.37558100	-1.88787300	0.67557900
C	1.53483800	-2.60192200	0.18657400
H	2.39270000	-1.91906100	0.16726600

H	1.32157300	-2.92728700	-0.83564200
C	1.74290700	-3.75802400	1.16399400
H	1.09757800	-4.60437700	0.90003000
H	2.77873300	-4.10967200	1.18025200
C	1.29308400	-3.13036300	2.49224900
H	0.99705700	-3.86950600	3.24264000
H	2.10210100	-2.52297200	2.91386400
C	0.11928500	-2.24580000	2.05785500
H	-0.83647700	-2.77674600	2.09902100
H	0.02840600	-1.32426900	2.64038000

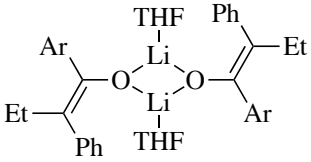


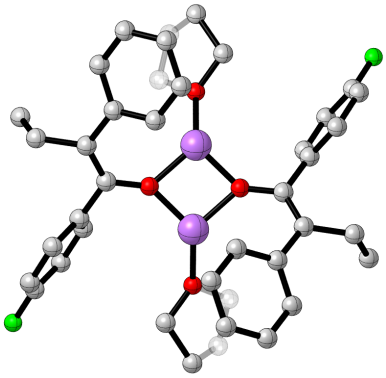


ZZ
G = –1601.167028
G_{MP2} = –1001576.849

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	1.27586000	0.79510200	-0.25996800
C	2.53669300	0.03356400	-0.43660000
C	2.88189800	-1.05677900	0.38795600
C	4.07363000	-1.76212600	0.20860300
C	4.97003300	-1.40640300	-0.80104300
C	4.64311100	-0.34536900	-1.65128200
C	3.44368000	0.35193000	-1.47788000
H	3.17222400	1.13764700	-2.18056700
H	5.30760800	-0.07592100	-2.46894300
H	5.89797100	-1.95449400	-0.93542700
H	4.30551500	-2.59362300	0.86968100
H	2.20961500	-1.34979600	1.18847700
C	1.32683400	2.16522400	-0.21577600
C	0.10057000	3.02508000	-0.13061800
C	-0.88845600	2.99941500	-1.12539800
C	-1.98724700	3.85834500	-1.07646700
C	-2.08991500	4.75012900	-0.01597000
C	-1.12827100	4.81293200	0.98695700
C	-0.03329100	3.95250700	0.91641500
H	0.72639600	3.98768800	1.69304200
H	-1.24700400	5.52104400	1.80087400
F	-3.15142500	5.58391400	0.04104600
H	-2.75220000	3.85012800	-1.84630200
H	-0.78646300	2.30955100	-1.95806600
O	2.46315900	2.85372200	-0.20076100
Li	3.27459200	4.46660900	-0.24373600
O	5.01078300	3.78594000	-0.19926800
C	6.14708100	4.47446200	-0.21526300
C	6.19805400	5.84457800	-0.26004900
C	4.93722600	6.60610900	-0.43654800
C	4.59244600	7.69692400	0.38757800
C	3.40073200	8.40230800	0.20831500
C	2.50390600	8.04618500	-0.80082200
C	2.83039800	6.98469700	-1.65065000
C	4.02981700	6.28734600	-1.47733700
H	4.30092300	5.50128000	-2.17977700
H	2.16558300	6.71490300	-2.46793800
H	1.57598700	8.59432300	-0.93514100
H	3.16919000	9.23416500	0.86906000
H	5.26506300	7.99027100	1.18769800
C	7.47402100	6.63972300	-0.00070300
C	7.90943100	6.70291300	1.47644600
H	7.13488800	7.14701100	2.11248900
H	8.82118700	7.30277600	1.59068800
H	8.11495100	5.69869600	1.86230100
H	8.30751900	6.22668200	-0.57855500
H	7.33441100	7.66106600	-0.37666500
C	7.37337900	3.61463000	-0.13031700
C	8.36219600	3.64019300	-1.12531600
C	9.46099900	2.78127100	-1.07653500
C	9.56389600	1.88959300	-0.01596900
C	8.60244900	1.82686800	0.98715000
C	7.50744600	2.68727400	0.91675500

H	6.74786700	2.65211200	1.69348000
H	8.72133800	1.11881200	1.80109400
F	10.6254230	1.05581900	0.04090300
H	10.2257850	2.78940800	-1.84653700
H	8.26002400	4.32995900	-1.95804300
Li	4.19923600	2.17313800	-0.24487400
C	-0.43494900	-0.06284300	1.47730300
H	0.33980500	-0.50677000	2.11320700
H	-1.34664900	-0.66270900	1.59197300
H	-0.64038400	0.94145700	1.86298600
H	-0.83368500	0.41289000	-0.57769900
H	0.13950900	-1.02143600	-0.37574700



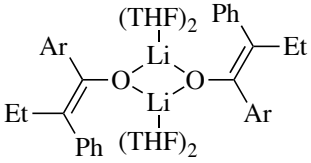


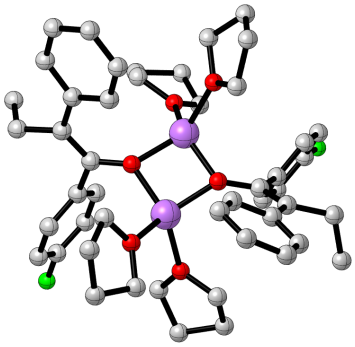
***ZZ*(THF)$_2$**
G = –2065.893509
G_{MP2} = –1292234.174

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	1.15597500	0.99628000	-0.03406800
C	2.39378300	0.58053800	-0.72907300
C	2.75043400	-0.78088300	-0.86071000
C	3.90378200	-1.18027700	-1.53764700
C	4.75178900	-0.23766300	-2.12178900
C	4.40863600	1.11506700	-2.03350100
C	3.25644200	1.51350500	-1.35665400
H	2.98537300	2.56377100	-1.34624000
H	5.02826800	1.86731700	-2.51711800
H	5.64571800	-0.54999100	-2.65491800
H	4.13557500	-2.24055200	-1.61356000
H	2.11594000	-1.54551500	-0.42429600
C	1.08697700	2.19249400	0.64646200
C	-0.19511900	2.68584800	1.26352000
C	-1.32162900	2.99048100	0.48407800
C	-2.48112500	3.51645100	1.05731400
C	-2.50581300	3.73398200	2.42938400
C	-1.40728000	3.45614800	3.23664500
C	-0.25392400	2.94419300	2.64247400
H	0.61921700	2.73844300	3.25494500
H	-1.46689200	3.63942700	4.30499700
F	-3.62693200	4.23471900	2.99663100
H	-3.35449000	3.75732600	0.45955900

Atom	X	Y	Z
H	-1.28576900	2.81942900	-0.58828200
O	2.11003300	3.00208500	0.85911500
Li	2.53757300	4.80703900	0.95395300
Li	3.96831700	2.70360100	0.95390200
O	4.39542600	4.50850600	0.85839500
C	5.41837100	5.31830700	0.64576400
C	5.34912400	6.51445200	-0.03485400
C	6.50471800	7.51116600	-0.00083400
C	6.56683800	8.38031300	1.27116500
H	5.64384200	8.95256900	1.42203100
H	7.39899600	9.09449000	1.22219400
H	6.71341500	7.75306200	2.15761400
H	7.46238400	6.99059800	-0.09109300
H	6.44354800	8.16427700	-0.88027900
C	4.11128800	6.92978500	-0.73007200
C	3.75412100	8.29107400	-0.86151600
C	2.60079300	8.69010600	-1.53872100
C	1.75340200	7.74725000	-2.12338900
C	2.09716900	6.39465000	-2.03537100
C	3.24927800	5.99658400	-1.35814300
H	3.52077500	4.94643000	-1.34782500
H	1.47819900	5.64222600	-2.51958500
H	0.85955200	8.05933700	-2.65678700
H	2.36853600	9.75029200	-1.61446300

H	4.38818900	9.05588800	-0.42477800
C	6.70047300	4.82531300	1.26303900
C	7.82717800	4.52094000	0.48376300
C	8.98676300	3.99537500	1.05718300
C	9.01132600	3.77792200	2.42926700
C	7.91260200	4.05548000	3.23636200
C	6.75918100	4.56708200	2.64201700
H	5.88590800	4.77262500	3.25437000
H	7.97212400	3.87227000	4.30473100
F	10.1325030	3.27753500	2.99669600
H	9.86027300	3.75471500	0.45955300
H	7.79140700	4.69192300	-0.58860900
C	-0.06244900	-0.86906400	1.27203700
H	0.86030900	-1.44170200	1.42289000
H	-0.89490800	-1.58289300	1.22312700
H	-0.20871600	-0.24172200	2.15847600
H	-0.95746800	0.52092300	-0.09031300
H	0.06091900	-0.65318000	-0.87941500
C	2.35873200	7.16868200	2.74316000
H	3.16085100	7.60847100	2.14036400
H	2.80166800	6.62417200	3.58251700
C	1.32110700	8.20971100	3.16650500
H	0.80012800	7.88675600	4.07555600
H	1.77159800	9.18739900	3.36137900
C	0.35954700	8.21239800	1.96748700
H	-0.63517700	8.59655000	2.21232700
H	0.77149500	8.81320000	1.14940400
C	0.32977300	6.73571200	1.57177500
H	-0.42492200	6.16895000	2.12841800
H	0.17992200	6.57802200	0.50048300
O	1.63815900	6.21575200	1.92317100
C	4.14899200	0.34125000	2.74222300
H	3.34696400	-0.09902200	2.13967900
H	3.70601100	0.88551500	3.58171700
C	5.18738900	-0.69914700	3.16529700
H	5.70809700	-0.37614900	4.07448700
H	4.73757900	-1.67722400	3.35983100
C	6.14907200	-0.70077700	1.96637200
H	7.14402300	-1.08435300	2.21121700
H	5.73762800	-1.30151900	1.14799700
C	6.17786000	0.77606900	1.57136200
H	6.93155300	1.34318300	2.12903100
H	6.32859200	0.93452800	0.50032100
O	4.86867900	1.29461900	1.92188000





***ZZ*(THF)$_4$**
G = –2530.586515
G_{MP2} = –1582873.513

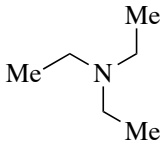
Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
O	-1.56963700	1.12253500	0.11812600
C	-2.83874200	0.82619600	-0.07278700
C	-3.91092200	1.24217000	0.69781500
C	-5.33719500	0.92719100	0.24772300
C	-5.98059600	1.99217900	-0.66317000
H	-5.97105000	2.98614600	-0.20194700
H	-7.02343500	1.73825400	-0.89383500
H	-5.43741300	2.06208900	-1.61304900
H	-5.36683600	-0.02241400	-0.29035600
H	-5.97359700	0.77719600	1.12867700
C	-3.76543200	2.05317100	1.92844700
C	-4.88195300	2.71068500	2.50318400
C	-4.78956600	3.44183800	3.68599100
C	-3.57629000	3.54774400	4.36595700
C	-2.45863800	2.90708700	3.82702100
C	-2.54418700	2.18885400	2.63522300
H	-1.66338900	1.70403100	2.24022300
H	-1.50369400	2.95561600	4.34723000
H	-3.50470400	4.10843500	5.29437900

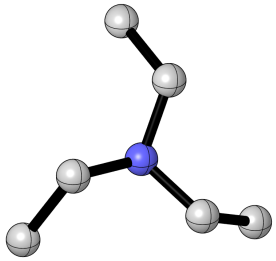
H	-5.67969800	3.92819900	4.07927200
H	-5.85043400	2.65577000	2.01992800
C	-3.06074200	-0.02336700	-1.30652600
C	-3.50044900	-1.35434400	-1.23637900
C	-3.66090700	-2.13035800	-2.38713100
C	-3.37526200	-1.55894200	-3.62134800
C	-2.91839200	-0.25064000	-3.73429500
C	-2.75191600	0.50265400	-2.57127800
H	-2.37412200	1.51888600	-2.63734700
H	-2.70324300	0.15857200	-4.71669600
F	-3.53900800	-2.29785500	-4.74318200
H	-4.00736800	-3.15803900	-2.33873900
H	-3.72939700	-1.78732500	-0.26643000
Li	-0.41002700	2.65843100	0.00219900
O	1.15979800	1.53567700	0.11744700
C	2.42876900	1.83299000	-0.07276200
C	3.50114500	1.41585200	0.69692500
C	4.92723100	1.73244500	0.24736200
C	5.57122900	0.66927900	-0.66525600
H	5.56207300	-0.32546300	-0.20570600
H	6.61397800	0.92407100	-0.89537300
H	5.02819300	0.60072200	-1.61532100
H	4.95627000	2.68292200	-0.28920100
H	5.56355900	1.88140700	1.12854700
C	3.35613600	0.60231700	1.92593600
C	4.47315400	-0.05524900	2.49966200
C	4.38123800	-0.78870300	3.68107600
C	3.16793600	-0.89702600	4.36061300
C	2.04977900	-0.25646700	3.82262300
C	2.13486900	0.46407900	2.63218200
H	1.25362400	0.94868700	2.23792900
H	1.09477400	-0.30692400	4.34253300
H	3.09669100	-1.45952900	5.28796400
H	5.27175700	-1.27495500	4.07361200
H	5.44167600	0.00147500	2.01670200
C	2.65041700	2.68555500	-1.30450900
C	3.08878300	4.01680100	-1.23105300
C	3.24902700	4.79566500	-2.37990800
C	2.96449100	4.22687700	-3.61560200
C	2.50897800	2.91839400	-3.73180600
C	2.34274800	2.16220200	-2.57062800
H	1.96624000	1.14567400	-2.63940500
H	2.29469300	2.51123200	-4.71524500
F	3.12805100	4.96857200	-4.73561500
H	3.59452900	5.82354500	-2.32893900
H	3.31697000	4.44770700	-0.26000400
O	-1.29610000	3.87589300	-1.42931700
C	-0.69520600	4.42165300	-2.62712300
H	-0.48780200	3.59637600	-3.31823600
H	0.25518400	4.88940200	-2.35803600
C	-1.72477200	5.39699200	-3.20521300
H	-1.59446700	6.39645800	-2.77270300
H	-1.64633800	5.48794300	-4.29268800
C	-3.05211200	4.78203900	-2.73427300
H	-3.88002900	5.49700800	-2.71452700
H	-3.34117100	3.94628200	-3.38292600
C	-2.68513900	4.27613600	-1.33974500
H	-2.77750800	5.07538100	-0.59248800
H	-3.26294100	3.41416100	-1.00095000
O	0.05858300	4.17618100	1.30260200
C	-0.59525200	5.45345800	1.41156000
H	-1.57788300	5.32221800	1.88501800
H	-0.73197200	5.83953400	0.39914300
C	0.33355200	6.29925500	2.27983900
H	1.16048100	6.69418800	1.67750800
H	-0.18050500	7.14174500	2.75269000
C	0.84309700	5.25607700	3.28643800
H	1.80229600	5.52313400	3.73969400
H	0.11257600	5.12781500	4.09298600
C	0.93714500	3.97748500	2.43943600
H	1.94418400	3.79496500	2.05280300
H	0.61525700	3.08709400	2.98528200
O	0.88577500	-1.21573800	-1.43359000
C	0.28397100	-1.75918700	-2.63202100
H	0.07372300	-0.93225700	-3.32024100
H	-0.66506600	-2.22959100	-2.36274500
C	1.31445100	-2.73083400	-3.21470600
H	1.18658300	-3.73192800	-2.78526600
H	1.23461000	-2.81840100	-4.30235900
C	2.64136600	-2.11500700	-2.74375500
H	3.47058800	-2.82855400	-2.72747700
H	2.92798100	-1.27666100	-3.39014100
C	2.27552500	-1.61411900	-1.34711900
H	2.37023000	-2.41558800	-0.60251800
H	2.85249000	-0.75232300	-1.00643700
O	-0.46810500	-1.52013700	1.29735300
C	0.18766800	-2.79659500	1.40442000
H	1.16961500	-2.66481100	1.87913100
H	0.32594700	-3.18026300	0.39133100
C	-0.74081200	-3.64548300	2.26999100
H	-1.56665800	-4.04015900	1.66601500
H	-0.22609300	-4.48835000	2.74145300

C	-1.25263500	-2.60523200	3.27849400
H	-2.21222600	-2.87431000	3.72971700
H	-0.52341000	-2.47839900	4.08643000

C	-1.34665200	-1.32440800	2.43470300
H	-2.35361200	-1.14077100	2.04844200
H	-1.02476000	-0.43550800	2.98301200

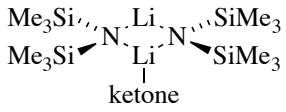
Table A.1.4. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant ground states of LiHMDS/Et_3N-mediated enolizations at 0 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

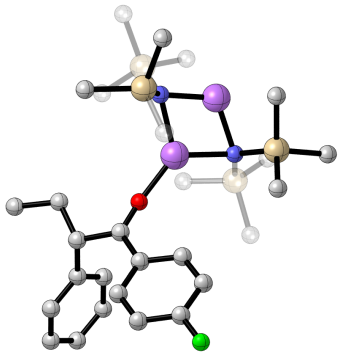




Et_3N
G = –292.239430
G_{MP2} = –182700.382

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
N	-1.38927400	0.20827400	-0.42731300
C	-1.90313600	1.51608700	-0.00137700
H	-1.07882400	2.23469400	-0.05273200
H	-2.22539600	1.49514800	1.05887400
C	-3.04066100	2.02960600	-0.88649400
H	-3.36786900	3.02070100	-0.55047400
H	-2.70645100	2.10530100	-1.92635000
H	-3.91519900	1.37000000	-0.86257400
C	-2.26438800	-0.89066900	0.00029400
H	-2.08172900	-1.16094400	1.05949300
H	-3.29896600	-0.53576800	-0.04688000
C	-2.14435300	-2.13146800	-0.88696600
H	-1.13625200	-2.56010900	-0.86680000
H	-2.83884300	-2.91015100	-0.54994500
H	-2.37986900	-1.87821600	-1.92576500
H	0.20957600	-1.07345600	-0.04735800
H	0.14273500	0.29346000	1.05918500
C	1.01423700	0.72440600	-0.88743600
H	2.03578200	0.51384400	-0.54928100
H	0.91387300	0.39235600	-1.92588500
H	0.87995900	1.81157400	-0.86863300

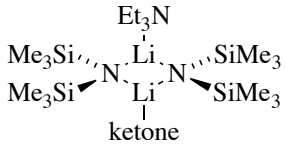


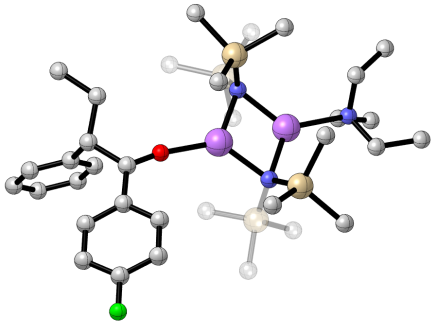


A_2(ketone)
G = –2555.038917
G_{MP2} = –1599012.756

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	-1.20516000	0.86928400	-1.19132800
H	-2.08797700	1.23017100	-0.64712100
H	-0.73750400	1.73908200	-1.67041000
H	-1.55102700	0.19960200	-1.98793700
C	0.65059800	1.35379100	1.16944400
H	-0.13724600	1.77522300	1.80507800
H	1.43898300	0.97380200	1.82994300
H	1.07669200	2.18161700	0.58760300
N	-0.63002700	-1.42408500	0.74565900
Si	-1.33816300	-1.42796800	2.32455000
C	-0.11687000	-1.07542300	3.74385300

H	0.74369400	-1.75624300	3.70551700
H	0.27312800	-0.05207000	3.71504700
H	-0.60177600	-1.21506200	4.71912700
C	-2.05811400	-3.15224100	2.71132800
H	-2.58053600	-3.12975900	3.67672100
H	-2.78246800	-3.49157300	1.96029200
H	-1.27794300	-3.91920000	2.78745600
C	-2.77886500	-0.19221700	2.50999300
H	-2.44893500	0.84418300	2.36432600
H	-3.57216200	-0.38671900	1.77626300
H	-3.23185200	-0.25031100	3.50839400
Li	0.76541000	-2.62521300	0.06168700
N	0.03658600	-4.12952100	-0.94568100
Si	-0.12411800	-4.23018200	-2.66313600
C	1.52409700	-4.09086500	-3.60875300
H	2.19540900	-4.92767000	-3.38400000
H	1.35986400	-4.08328400	-4.69437800
H	2.05655200	-3.16595000	-3.35093500
C	-1.20464100	-2.78797000	-3.29130100
H	-1.30680500	-2.83702200	-4.38310200
H	-2.21977100	-2.81362600	-2.87405900
H	-0.77086300	-1.80875900	-3.05318500
C	-0.97854600	-5.82307600	-3.26944700
H	-0.40612000	-6.72280000	-3.01300400
H	-1.97454700	-5.93273500	-2.82105400
H	-1.10571200	-5.81786000	-4.35992400
Si	0.71264900	-5.37840300	0.03589800
C	-0.58461100	-6.51460400	0.83697500
H	-1.32566900	-5.94294300	1.40858100
H	-1.12804200	-7.07675100	0.06699500
H	-0.12678200	-7.24333800	1.51841400
C	1.68511600	-4.53281100	1.46500000
H	2.08968800	-5.29284100	2.14526200
H	2.55705600	-3.96874500	1.09441200
H	1.08017700	-3.85888400	2.08785100
C	1.99463900	-6.51060300	-0.80059400
H	1.56802100	-7.09608400	-1.62373600
H	2.83599100	-5.93601700	-1.20697100
H	2.40297500	-7.22408300	-0.07288700
Li	-1.54713900	-2.99228300	-0.27029600
O	-3.44139700	-3.35445900	-0.50291100
C	-4.61354000	-3.39008700	-0.88943100
C	-5.43969100	-4.66741700	-0.69092500
C	-6.50752600	-4.43649200	0.38006100
C	-6.15269400	-3.97004400	1.65401400
C	-7.12322300	-3.78329900	2.63868300
C	-8.46376400	-4.06375300	2.36807500
C	-8.82712800	-4.53508200	1.10598400
C	-7.85524900	-4.71725000	0.12093700
H	-8.14704800	-5.09184100	-0.85807300
H	-9.86661800	-4.76333000	0.88600400
H	-9.21877100	-3.91798100	3.13561700
H	-6.82933900	-3.41796700	3.61889600
H	-5.11242300	-3.75463900	1.88307300
C	-4.53987400	-5.88499300	-0.38589300
C	-5.30494200	-7.21123500	-0.38079300
H	-6.08671900	-7.22582500	0.38585300
H	-5.78228300	-7.40256300	-1.35034900
H	-4.62181700	-8.04310900	-0.17934800
H	-3.74003000	-5.92298900	-1.13452300
H	-4.04443300	-5.73390600	0.57887600
H	-5.95972400	-4.86411800	-1.63798600
C	-5.22348400	-2.19249700	-1.52382900
C	-6.47778300	-2.22048800	-2.16098900
C	-6.99908100	-1.07825100	-2.75830300
C	-6.25875500	0.09957200	-2.70695200
C	-5.01778700	0.16950500	-2.07914800
C	-4.50692200	-0.98062500	-1.49253700
H	-3.54514400	-0.94777500	-0.99375600
H	-4.47263800	1.10694000	-2.05940800
F	-6.76096900	1.20441100	-3.28070800
H	-7.96187200	-1.08477900	-3.25768200
H	-7.05979200	-3.13334500	-2.19423700
C	1.53108000	-0.51080800	-1.04596300
H	2.36074200	-0.88335200	-0.42214200
H	1.31842000	-1.26204800	-1.81910900
H	1.92959000	0.36454800	-1.57393300

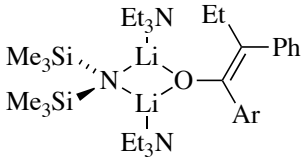


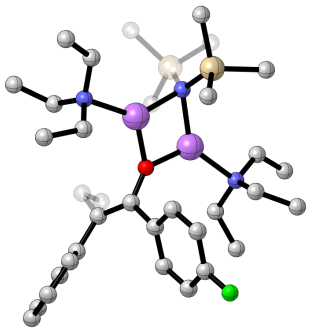


A_2(ketone)(Et_3N)
G = –2847.248092
G_{MP2} = –1781706.525

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	-1.42288300	0.87937800	-0.92199800
H	-2.10869400	1.37489300	-0.22383800
H	-1.02691500	1.65202700	-1.59413900
H	-2.00825200	0.18472300	-1.53824100
C	1.00576100	1.41501600	0.80013400
H	0.40957100	2.01030500	1.50076900
H	1.88233200	1.05192000	1.34926400
H	1.36824200	2.10055100	0.02260900
N	-0.50518700	-1.25987300	1.07744800
Si	-1.08391000	-0.86672800	2.66558100
C	0.30481600	-0.77387400	3.96926700
H	0.84486100	-1.72607600	4.05114400
H	1.03772500	0.00173400	3.71558100
H	-0.09377400	-0.53994300	4.96512900
C	-2.31209400	-2.19187600	3.27836800
H	-2.51010800	-2.05394900	4.34929100
H	-3.27305600	-2.10781000	2.75761700
H	-1.94696100	-3.21734400	3.15213200
C	-2.06758900	0.76140000	2.83003400
H	-1.47909000	1.65683600	2.60263300
H	-2.94721400	0.76622700	2.17525000
H	-2.43146900	0.86590800	3.86087300
Li	-1.65248600	-2.87828100	0.47800500
Li	0.80244500	-2.83862200	0.91098400
N	3.14191100	-2.87208800	1.49935600
C	3.65054600	-3.55143200	0.28648100
H	2.91792800	-4.31927700	0.01382200
H	3.62766600	-2.80909500	-0.51996800
C	5.03560000	-4.22020200	0.31317000
H	5.84088400	-3.52749100	0.57153800
H	5.06545500	-5.05885800	1.01627300
H	5.24727900	-4.62627100	-0.68347500
C	3.54426100	-1.45662300	1.64916900
H	3.17185700	-1.12844500	2.62600600
H	2.98797500	-0.87838000	0.90488000
C	5.02763600	-1.07338000	1.50879000
H	5.12907600	0.00486500	1.68282500
H	5.67599000	-1.58998400	2.22106400
H	5.40130800	-1.27323400	0.49933100
C	3.21046700	-3.66586100	2.74406000
H	2.41367600	-3.30066400	3.40343900
H	2.94229000	-4.69378900	2.47863400
C	4.50811200	-3.67396100	3.57217100
H	4.73594700	-2.68193200	3.97502800
H	4.37188800	-4.34673600	4.42778100
H	5.37678400	-4.02194800	3.00763800
N	-0.31303800	-4.41616300	0.18600900
Si	-0.39430400	-4.63932600	-1.53390600
C	1.28742500	-4.48834400	-2.42091300
H	1.97652600	-5.27606500	-2.09131300
H	1.16259900	-4.59696400	-3.50639700
H	1.77515100	-3.52346300	-2.24276400
C	-1.55185100	-3.33555400	-2.32363400
H	-1.44184200	-3.34678400	-3.41580900
H	-2.60115900	-3.56266400	-2.09989600
H	-1.35875000	-2.30553500	-1.99980500
C	-1.10827400	-6.30056200	-2.14600100
H	-0.51628800	-7.16712700	-1.82853300
H	-2.13657300	-6.45698800	-1.80046600
H	-1.12632400	-6.30577600	-3.24407600
Si	-0.20518200	-5.78146700	1.24573900
C	-1.71076600	-6.95290900	1.27988300
H	-2.63270400	-6.41760600	1.53856300
H	-1.87972900	-7.46709900	0.32821400
H	-1.56106100	-7.72514600	2.04695900
C	-0.04114200	-5.23806500	3.07446200
H	0.53441500	-5.98278900	3.63992800
H	0.45254000	-4.27148500	3.22207400
H	-1.02533100	-5.16915700	3.55323500

C	1.28923100	-6.92045100	0.88852000
H	1.24726800	-7.34339300	-0.12294200
H	2.24836700	-6.39473300	0.97707300
H	1.31213700	-7.76297300	1.59235400
O	-3.65452200	-3.08935100	0.28962300
C	-4.88381900	-3.00029000	0.22899200
C	-5.73955500	-4.26921300	0.12222300
C	-6.21432800	-4.69900600	1.51217700
C	-5.30773400	-4.86173700	2.56960700
C	-5.74839600	-5.28285700	3.82479900
C	-7.10091800	-5.54966400	4.04435200
C	-8.01155500	-5.39403200	2.99856700
C	-7.57002000	-4.96991300	1.74426900
H	-8.28567200	-4.85896700	0.93200900
H	-9.06624700	-5.60370500	3.15597300
H	-7.44221000	-5.87691700	5.02257400
H	-5.03085100	-5.40025900	4.63219700
H	-4.25324400	-4.65494800	2.41467600
C	-4.98268300	-5.38952200	-0.62868500
C	-5.84992000	-6.61878000	-0.91142200
H	-6.20555600	-7.08413700	0.01363700
H	-6.72818700	-6.36190900	-1.51735500
H	-5.27497300	-7.36945200	-1.46417600
H	-4.61178000	-4.97803700	-1.57592400
H	-4.09920600	-5.67621500	-0.05199600
H	-6.62971900	-4.01788200	-0.46632400
C	-5.54486200	-1.66859500	0.24547300
C	-6.92917600	-1.51062700	0.44357600
C	-7.50805600	-0.24616100	0.44629700
C	-6.69341000	0.86182700	0.23033300
C	-5.32096900	0.74519700	0.02725600
C	-4.75326100	-0.52253200	0.04690100
H	-3.68614600	-0.63712100	-0.10015000
H	-4.72161400	1.63319500	-0.14191900
F	-7.25200200	2.08301400	0.21779800
H	-8.57093600	-0.10604300	0.61129400
H	-7.56014800	-2.37161200	0.62974900
C	1.12257800	-0.66809100	-1.39458400
H	2.02004400	-1.18183300	-1.02745200
H	0.60299200	-1.36055100	-2.06434800
H	1.47300600	0.17170200	-2.00917100

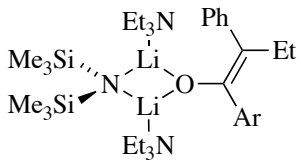


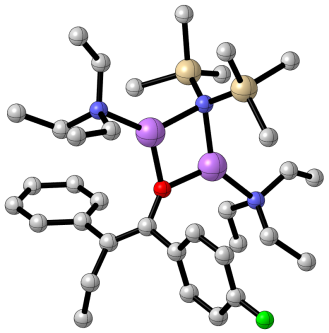


AE(Et_3N)$_2$
G = –2265.766766
G_{MP2} = –1417487.288

Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
N	1.67243900	-1.14966200	-0.16250500
Si	2.52919300	-0.88053600	-1.64019900
C	3.05727200	0.93523300	-1.90026500
H	3.70484500	1.28680200	-1.08813400
H	3.60837700	1.05997400	-2.84165600
H	2.18916100	1.60669600	-1.94266700
C	1.40359200	-1.30167800	-3.12173100
H	1.91687900	-1.08879300	-4.06837200
H	1.12097200	-2.36332400	-3.14764600
H	0.47409100	-0.71908200	-3.11681400
C	4.11127900	-1.92207100	-1.86556300
H	4.88271600	-1.67511000	-1.12545400
H	3.90665300	-2.99649800	-1.77792700
H	4.54754200	-1.74935500	-2.85810500
Si	2.46544100	-1.31263800	1.36355000
C	3.29655800	-3.00543100	1.65485700
H	2.56636100	-3.82470700	1.66568700
H	4.03633700	-3.23319600	0.87861400
H	3.81642700	-3.02427200	2.62187800
C	1.18969700	-1.13576400	2.77435900
H	1.67668500	-1.24517900	3.75193200
H	0.69099900	-0.15659300	2.77593000
H	0.40592900	-1.90192200	2.71532800

C	3.82845900	-0.02030100	1.70089800
H	4.66985200	-0.12774900	1.00503900
H	3.45798900	1.00743900	1.60435700
H	4.23107100	-0.13329100	2.71599900
Li	0.11707600	-2.41497100	-0.50319300
O	-1.31561200	-1.24424600	-0.40668200
C	-2.65171700	-1.29690200	-0.39875700
C	-3.22142700	-2.07318000	0.75534500
C	-4.24202600	-3.02358800	0.57504000
C	-4.70982700	-3.79923200	1.63511800
C	-4.14825400	-3.62084600	2.89458200
C	-3.13030700	-2.70090400	3.11621800
C	-2.66788400	-1.94306900	2.04008600
H	-1.86081200	-1.23624800	2.19978000
H	-2.71279200	-2.59067000	4.11213800
F	-4.59656700	-4.36859400	3.92759100
H	-5.49585800	-4.53485200	1.49698600
H	-4.67639100	-3.15384400	-0.41042000
C	-3.42221200	-0.74645600	-1.39454700
C	-2.74148400	-0.24467000	-2.66131400
H	-1.78183400	0.21552600	-2.40098000
H	-3.35362900	0.54245700	-3.11921200
C	-2.46191900	-1.33794000	-3.71148300
H	-1.96235700	-0.91756800	-4.59348200
H	-1.81094300	-2.11280200	-3.29504700
H	-3.38248500	-1.82596400	-4.05037700
C	-4.89293200	-0.56177600	-1.30284000
C	-5.51821500	-0.12360400	-0.11577500
C	-6.89170400	0.09770300	-0.05005100
C	-7.69497600	-0.09048000	-1.17731000
C	-7.09768400	-0.49885600	-2.37020300
C	-5.72294700	-0.72662300	-2.43150500
H	-5.28803700	-1.04828600	-3.37276400
H	-7.70392500	-0.64463400	-3.26131600
H	-8.76574700	0.08888600	-1.12865800
H	-7.33472800	0.43545100	0.88398800
H	-4.90966200	0.05310200	0.76556500
N	-0.08725300	-4.54745200	-0.71138500
C	-0.41128400	-4.87199400	0.69788800
H	0.23832700	-4.25345800	1.33363400
H	-1.43328400	-4.52078400	0.87315600
C	-0.27353500	-6.32366000	1.18363400
H	-0.89278900	-7.02129700	0.61386200
H	0.76446500	-6.66862700	1.13713600
H	-0.58760100	-6.37522700	2.23302200
C	-1.21003400	-4.68297900	-1.66800900
H	-0.79480800	-4.48850200	-2.66473200
H	-1.91388500	-3.86767700	-1.46282000
C	-2.01492000	-5.99255800	-1.69584500
H	-2.76856600	-5.92624900	-2.48983800
H	-1.39573200	-6.87177400	-1.89247000
H	-2.55026700	-6.15145300	-0.75436600
C	1.22414000	-5.03281500	-1.19673000
H	1.56280000	-4.33352400	-1.97269300
H	1.92740900	-4.92187300	-0.36450400
C	1.33211900	-6.45270100	-1.77656200
H	0.73088000	-6.56394600	-2.68449700
H	2.37635300	-6.64189000	-2.05353700
H	1.02769500	-7.22694600	-1.06749500
N	-0.45986800	2.07623000	0.47045100
C	0.78025200	2.63927700	1.05054100
H	1.20631100	1.87437800	1.71155200
H	1.48954800	2.75125500	0.22294500
C	0.71155000	3.95029200	1.85136400
H	0.30480900	4.78449100	1.27404000
H	0.11082900	3.83625800	2.75932000
H	1.72624200	4.22251200	2.16631300
C	-0.82328600	2.58120400	-0.87339400
H	-1.79885300	2.14701400	-1.11457300
H	-0.10853500	2.15139100	-1.59010700
C	-0.85928100	4.09765300	-1.12180200
H	-1.17806200	4.27766500	-2.15549300
H	-1.55606300	4.61894400	-0.46034100
H	0.13067800	4.54979600	-1.00353000
C	-1.59411400	1.91909600	1.40983700
H	-2.20245600	1.08357900	1.04184200
H	-1.16297900	1.59774400	2.36646000
C	-2.54239300	3.10535100	1.65120200
H	-3.08905500	3.37293100	0.74143700
H	-3.28779900	2.81257600	2.40034300
H	-2.02827000	3.99693100	2.01903800



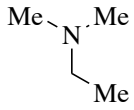


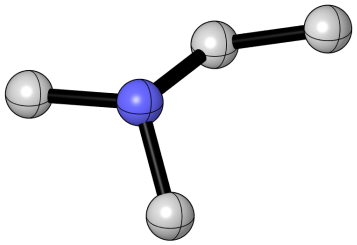
AZ(Et_3N)$_2$
G = –2265.761719
G_{MP2} = –1417484.981

Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
N	-1.03479700	1.76899500	0.18336900
Si	-0.25217600	2.63677200	1.46182300
C	0.93614000	4.01758700	0.89201900
H	0.42104400	4.82275000	0.35469000
H	1.43595500	4.47286200	1.75721000
H	1.71977000	3.63116200	0.22858300
C	0.81463400	1.44757800	2.49962500
H	0.26173300	0.56599000	2.84362600
H	1.69462300	1.08569900	1.95125400
H	1.19433300	1.96020500	3.39310700
C	-1.44091000	3.46373700	2.70529200
H	-2.10690100	4.18822100	2.22106000
H	-2.07122400	2.72694700	3.22056200
H	-0.87926400	4.00302700	3.47956000
Si	-1.62986000	2.59068100	-1.21955100
C	-2.49821700	4.25507900	-0.87562200
H	-3.34880900	4.13374900	-0.19359400
H	-1.82653200	4.99849200	-0.43034800
H	-2.88593000	4.68507800	-1.80855100
C	-2.94013200	1.52591400	-2.10903700
H	-3.24987200	2.01549400	-3.04147800
H	-2.57292800	0.52803900	-2.37461700
H	-3.85078900	1.39184100	-1.51002700
C	-0.30551600	2.95814500	-2.54300400
H	0.49426700	3.60123700	-2.15647500
H	0.16195500	2.03699600	-2.91497100
H	-0.74733700	3.46883800	-3.40881200
Li	-2.38794700	0.29289400	0.58590000
O	-1.34530700	-1.24971700	0.38432400
C	-1.52823300	-2.56344200	0.21953800
C	-2.56866500	-2.89587600	-0.81929000
C	-3.65403300	-3.74364100	-0.54011200
C	-4.64382300	-4.00332000	-1.48965900
C	-4.54374300	-3.40315800	-2.73863800
C	-3.49111100	-2.55241200	-3.05730400
C	-2.51945200	-2.29956100	-2.08991000
H	-1.69853100	-1.63101200	-2.32764200
H	-3.44442500	-2.10255900	-4.04393300
F	-5.49473800	-3.64958500	-3.66635400
H	-5.48320300	-4.65660100	-1.27315900
H	-3.72639500	-4.20570900	0.43967700
C	-0.85007800	-3.55336700	0.89466400
C	0.05717200	-3.26752000	2.03704500
C	1.20566800	-4.05261200	2.27942200
C	2.03086500	-3.83218100	3.38248400
C	1.73319600	-2.82339600	4.29918800
C	0.59497200	-2.04143400	4.08982900
C	-0.22150300	-2.25723600	2.98103900
H	-1.10195800	-1.64240600	2.83985500
H	0.33653500	-1.25877200	4.79931100
H	2.36885100	-2.65535200	5.16440100
H	2.90706900	-4.46005900	3.52782800
H	1.46454600	-4.85316300	1.59345700
C	-0.94808200	-5.01816400	0.48059400
H	0.05321800	-5.39031900	0.21738600
H	-1.52897700	-5.11047400	-0.43923500
C	-1.53688300	-5.95841800	1.54755600
H	-1.54250100	-6.99666600	1.19347600
H	-0.95777000	-5.92229500	2.47620300
H	-2.56908500	-5.68261900	1.79501900
N	-4.36260800	0.32881200	1.50693900
C	-5.17137100	-0.58676600	0.67030700
H	-4.93978400	-0.36244000	-0.37930300
H	-4.78995000	-1.59669100	0.84958300
C	-6.70148600	-0.58140700	0.81675800
H	-7.03383200	-0.80724200	1.83359400
H	-7.13327400	0.38053600	0.52166600
H	-7.11953900	-1.34326400	0.14796800
C	-3.97413200	-0.20411400	2.83221500
H	-3.43795900	0.60169300	3.34905000
H	-3.24120000	-1.00266700	2.65555100

C	-5.05563400	-0.77618700	3.76426300
H	-4.58294600	-1.08879100	4.70317200
H	-5.83723400	-0.05158400	4.00560600
H	-5.53025300	-1.66178800	3.33009700
C	-4.78252900	1.74866800	1.48313800
H	-3.88371100	2.35687900	1.63514900
H	-5.12043200	1.95486600	0.46088600
C	-5.85037400	2.23224200	2.47742200
H	-5.50160000	2.15533500	3.51227700
H	-6.05688200	3.29195800	2.28455800
H	-6.79305000	1.68538900	2.39140800
N	1.91083900	-0.49342500	-0.91783900
C	1.43110900	-1.06376000	-2.19533100
H	0.53764600	-1.65918200	-1.96559900
H	1.09624500	-0.21929700	-2.81097300
C	2.36791100	-1.95874400	-3.02502600
H	3.29473600	-1.45622400	-3.31298400
H	2.62654400	-2.87470100	-2.48496100
H	1.84771000	-2.25886300	-3.94286600
C	2.65309200	0.78281800	-1.02438700
H	3.01325800	1.01665200	-0.01589600
H	1.92564500	1.56278600	-1.27748000
C	3.82169700	0.89222500	-2.01712800
H	4.27726800	1.88493800	-1.91731200
H	4.60095500	0.14571500	-1.84275400
H	3.48104900	0.79689300	-3.05320600
C	2.46493400	-1.47676800	0.04241000
H	2.27237200	-1.09528700	1.05319200
H	1.85632900	-2.38084000	-0.05221500
C	3.95499100	-1.84388000	-0.03473700
H	4.59744000	-0.98311400	0.17942300
H	4.16255600	-2.60178300	0.72966000
H	4.24605300	-2.25420900	-1.00561900

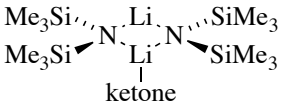
Table A.1.5. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant ground states of LiHMDS/DMEA-mediated enolizations at –40 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

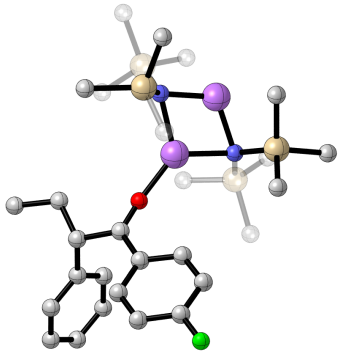




DMEA
G = –213.665394
G_{MP2} = –133579.161

Atom	X	Y	Z	Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000	H	3.83891700	1.79369500	0.24845300
N	1.20293200	0.78313000	-0.24712200	C	1.00890200	2.16718000	0.16436500
C	2.37351000	0.16464400	0.37745600	H	0.84479000	2.27734200	1.25589300
H	2.35555300	-0.89919700	0.11025300	H	1.87500300	2.77525100	-0.11147300
H	2.31330700	0.20948500	1.48541500	H	0.13541800	2.58100500	-0.35107400
C	3.70245400	0.76089600	-0.08917400	H	-0.84663300	0.44611100	-0.53359800
H	4.53704300	0.17458600	0.31158900	H	-0.27116100	-0.06399400	1.07339000
H	3.76283600	0.74780500	-1.18260600	H	0.13786100	-1.02018600	-0.37491000

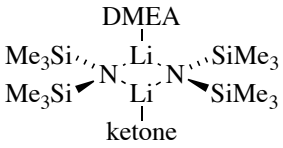


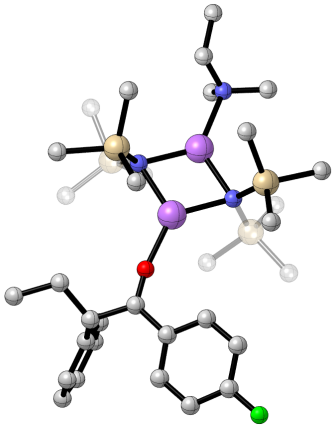


A_2(ketone)
G = –2555.021202
G_{MP2} = –1599001.640

Atom	X	Y	Z	Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000	Si	-1.33925900	-1.42607200	2.32498100
C	-1.20462300	0.86934900	-1.19181400	C	-0.11809200	-1.07332800	3.74434900
H	-2.08699400	1.23152500	-0.64773900	H	0.74218600	-1.75454100	3.70645500
H	-0.73626300	1.73831900	-1.67171200	H	0.27235700	-0.05016000	3.71516200
H	-1.55127300	0.19933200	-1.98780200	H	-0.60321800	-1.21234000	4.71960200
C	0.65112600	1.35402900	1.16888100	C	-2.05998900	-3.14983600	2.71257100
H	-0.13657300	1.77622900	1.80418600	H	-2.58260500	-3.12669000	3.67784100
H	1.43920700	0.97394400	1.82968700	H	-2.78428400	-3.48929500	1.96153700
H	1.07776400	2.18131900	0.58667700	H	-1.28005200	-3.91697600	2.78923900
N	-0.63076100	-1.42345800	0.74624800	C	-2.77943500	-0.18956200	2.50940400

H	-2.44899000	0.84661100	2.36329700
H	-3.57264900	-0.38406800	1.77558600
H	-3.23268600	-0.24695000	3.50772800
Li	0.76436300	-2.62551600	0.06319700
N	0.03506400	-4.12988600	-0.94379600
Si	-0.12523200	-4.23108600	-2.66125300
C	1.52326700	-4.09223700	-3.60645300
H	2.19460700	-4.92875700	-3.38070400
H	1.35943000	-4.08566300	-4.69214500
H	2.05552200	-3.16702800	-3.34928300
C	-1.20550700	-2.78897100	-3.29006600
H	-1.30719300	-2.83812600	-4.38190600
H	-2.22081400	-2.81458900	-2.87325000
H	-0.77182200	-1.80974500	-3.05184900
C	-0.97949400	-5.82409900	-3.26748500
H	-0.40707300	-6.72375800	-3.01081400
H	-1.97561800	-5.93379700	-2.81938800
H	-1.10633900	-5.81898300	-4.35800100
Si	0.71026600	-5.37862300	0.03856000
C	-0.58779100	-6.51355700	0.84013200
H	-1.32814300	-5.94109000	1.41184100
H	-1.13196500	-7.07537800	0.07044200
H	-0.13042600	-7.24254400	1.52161400
C	1.68285900	-4.53280800	1.46744100
H	2.08673900	-5.29271900	2.14824800
H	2.55525900	-3.96945800	1.09685300
H	1.07811100	-3.85820300	2.08975300
C	1.99175100	-6.51202000	-0.79708100
H	1.56486800	-7.09779400	-1.61987600
H	2.83342400	-5.93813400	-1.20378600
H	2.39968100	-7.22525300	-0.06890700
Li	-1.54835800	-2.99179200	-0.26917300
O	-3.44276700	-3.35344100	-0.50187300
C	-4.61496500	-3.38878200	-0.88826600
C	-5.44105400	-4.66629700	-0.69066800
C	-6.50881300	-4.43640900	0.38061600
C	-6.15398000	-3.97073100	1.65484100
C	-7.12445000	-3.78498600	2.63976200
C	-8.46492900	-4.06570600	2.36913700
C	-8.82829200	-4.53630800	1.10677000
C	-7.85647800	-4.71746500	0.12147800
H	-8.14826600	-5.09149900	-0.85774900
H	-9.86773200	-4.76477100	0.88677100
H	-9.21988800	-3.92071400	3.13687200
H	-6.83055900	-3.42022900	3.62018600
H	-5.11375500	-3.75516200	1.88394200
C	-4.54111100	-5.88405500	-0.38671500
C	-5.30605700	-7.21037100	-0.38269000
H	-6.08775900	-7.22570500	0.38401700
H	-5.78347200	-7.40089600	-1.35236800
H	-4.62283500	-8.04235800	-0.18203800
H	-3.74131800	-5.92134200	-1.13543100
H	-4.04561000	-5.73373100	0.57814400
H	-5.96115400	-4.86223700	-1.63785300
C	-5.22494900	-2.19076000	-1.52181100
C	-6.47975200	-2.21806900	-2.15801200
C	-7.00108900	-1.07543200	-2.75452500
C	-6.26026900	0.10209000	-2.70337900
C	-5.01876900	0.17133800	-2.07655000
C	-4.50789800	-0.97917200	-1.49069400
H	-3.54571400	-0.94686300	-0.99266800
H	-4.47323300	1.10855100	-2.05697000
F	-6.76249300	1.20729700	-3.27641800
H	-7.96428700	-1.08142100	-3.25312500
H	-7.06215700	-3.13068000	-2.19105100
C	1.53099900	-0.51190100	-1.04554800
H	2.36052500	-0.88423500	-0.42142300
H	1.31824400	-1.26357900	-1.81823600
H	1.92974000	0.36303500	-1.57403900





A_2(ketone)(DMEA)
G = –2768.666975
G_{MP2} = –1732580.281

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	-1.38085100	0.84873500	-1.00945300
H	-2.10760500	1.34723800	-0.35616600
H	-0.96107300	1.61568800	-1.67357800
H	-1.92719600	0.13726600	-1.64213500
C	0.94684200	1.42946500	0.84424100
H	0.31938100	2.00782700	1.53120500
H	1.81099500	1.07248400	1.41677800
H	1.32403900	2.12801600	0.08549400
N	-0.55071000	-1.25626200	1.05700000
Si	-1.21944300	-0.86426100	2.60833100
C	0.09401300	-0.73889900	3.98671200
H	0.65189400	-1.67795600	4.09797600
H	0.81915500	0.05709700	3.77665600
H	-0.36516300	-0.51781100	4.95912000
C	-2.45205900	-2.20800600	3.16898200
H	-2.72374200	-2.05172300	4.22110800
H	-3.37910500	-2.16348500	2.58560900
H	-2.05099200	-3.22483200	3.09181300
C	-2.23908600	0.74713800	2.71057500
H	-1.65995500	1.65087900	2.49170400
H	-3.09338800	0.72516300	2.02313200
H	-2.64396200	0.85967000	3.72518700
C	1.22042000	-0.66038800	-1.31284200
H	2.11998700	-1.10799700	-0.87233800
H	0.77720400	-1.40525900	-1.98095200
H	1.56139300	0.17339500	-1.94073300
Li	0.79558500	-2.81756200	0.94709400
Li	-1.63909500	-2.89451700	0.41170200
N	-0.27291200	-4.41433400	0.19490500
Si	-0.25164900	-4.66420500	-1.52173600
C	1.48564800	-4.53402100	-2.29793100
H	2.15604800	-5.29830700	-1.88479500
H	1.44077000	-4.68892800	-3.38406000
H	1.95027400	-3.55639700	-2.12614700
C	-1.35059600	-3.37018400	-2.40556400
H	-1.16763800	-3.39890900	-3.48773600
H	-2.41361500	-3.59088000	-2.25009200
H	-1.17743300	-2.33570500	-2.08530700
C	-0.93520300	-6.33327300	-2.14813200
H	-0.36017500	-7.19615800	-1.79187400
H	-1.97887400	-6.48473200	-1.84943000
H	-0.90063900	-6.35204900	-3.24567700
Si	-0.17983500	-5.75979600	1.27872100
C	-1.66980800	-6.95114200	1.27537200
H	-2.60758000	-6.42529400	1.49355000
H	-1.79668200	-7.47515300	0.32229100
H	-1.53976300	-7.71511200	2.05416300
C	-0.08158200	-5.18539200	3.10368400
H	0.48899600	-5.91081400	3.69860300
H	0.39062900	-4.20764100	3.25018100
H	-1.08074500	-5.12672800	3.55161900
C	1.34218100	-6.88324100	0.99221400
H	1.34533000	-7.31960400	-0.01420900
H	2.29117300	-6.34469200	1.11022400
H	1.34929300	-7.71635800	1.70752700
O	-3.61727600	-3.13254400	0.10587300
C	-4.84270500	-3.06944000	-0.02460100
C	-5.66292500	-4.35702300	-0.17416000
C	-6.20798800	-4.79061300	1.18868400
C	-5.36101400	-4.92734500	2.29785000
C	-5.86391000	-5.35357200	3.52767500
C	-7.22037900	-5.65089200	3.67000000
C	-8.07210400	-5.52057400	2.57236300
C	-7.56827700	-5.09156100	1.34343900
H	-8.23787700	-5.00078000	0.49046100
H	-9.12907200	-5.75403100	2.66945500
H	-7.61022400	-5.98219600	4.62851400

H	-5.19185400	-5.45097400	4.37584600
H	-4.30447900	-4.69626700	2.20312800
C	-4.83900600	-5.46285700	-0.87397100
C	-5.66011000	-6.71289300	-1.19991600
H	-6.05704000	-7.18360100	-0.29461200
H	-6.50810200	-6.47855700	-1.85610900
H	-5.03736400	-7.45164100	-1.71573500
H	-4.42397100	-5.04671000	-1.80063800
H	-3.98340800	-5.72656700	-0.24644800
H	-6.52282100	-4.12932700	-0.81485500
C	-5.53094600	-1.75173000	-0.04822800
C	-6.92870700	-1.62294100	0.05228800
C	-7.53221400	-0.37043800	0.02015900
C	-6.72712700	0.75510900	-0.13110800
C	-5.34158800	0.66754600	-0.23663700
C	-4.75079900	-0.58859800	-0.18397200
H	-3.67361500	-0.68100900	-0.25472400
H	-4.75029600	1.56881200	-0.35711700
F	-7.30833400	1.96492000	-0.17618000
H	-8.60679700	-0.25282300	0.10961900
H	-7.55381900	-2.49749500	0.18817500
N	2.98639600	-2.80294100	1.60956700
C	3.12883400	-3.59965000	2.83924800
H	2.48051600	-3.18459300	3.61626700
H	4.16007300	-3.59785900	3.22649300
H	2.82622800	-4.63241700	2.65170200
C	3.73668100	-3.40669300	0.47829200
H	3.53584500	-2.78788300	-0.40290800
H	3.28362200	-4.38363100	0.28220200
C	5.25557800	-3.56911500	0.63743800
H	5.66155800	-4.01309500	-0.27831100
H	5.76351600	-2.61115800	0.78994900
H	5.51985100	-4.23246800	1.46739500
C	3.41572500	-1.42053000	1.87819000
H	4.44597000	-1.36500700	2.26468400
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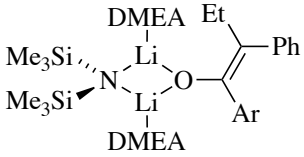
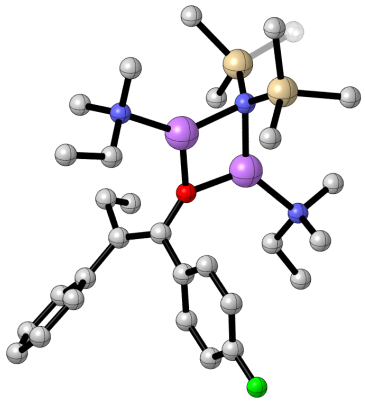
H	2.74781700	-0.97545400	2.61982100





AE(DMEA)$_2$
G = –2108.624965
G_{MP2} = –1319246.138

Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
N	1.66358300	1.14111800	0.20774900
Si	2.50915200	0.80346400	1.67633400
C	2.91868400	-1.04761600	1.89740700
H	3.54524400	-1.41740900	1.07633300
H	3.45746300	-1.23441100	2.83548200
H	2.00823000	-1.66203200	1.92061000
C	1.41502300	1.27982500	3.16411400
H	1.90273800	1.01216600	4.11025500
H	1.22281200	2.36144400	3.20213100
H	0.44176600	0.77429200	3.14379800
C	4.15312200	1.73985200	1.91124400
H	4.89704300	1.47578000	1.14957400
H	4.01109800	2.82691300	1.86678000
H	4.59278600	1.50522300	2.88948400
Si	2.45856100	1.37744200	-1.30569200
C	3.35149500	3.05481400	-1.48344800
H	2.65585100	3.89910800	-1.39071000
H	4.13056400	3.18619400	-0.72322900
H	3.83307400	3.14058600	-2.46655100
C	1.17329800	1.34344000	-2.71816700
H	1.65918100	1.48944600	-3.69141900
H	0.63254500	0.38818400	-2.77287400
H	0.42395400	2.13771000	-2.60673100

C	3.76479600	0.05403500	-1.73185200
H	4.59597900	0.05881400	-1.01560800
H	3.33909700	-0.95690300	-1.72734700
H	4.19288800	0.22836900	-2.72762100
Li	0.10852900	2.37584400	0.62950000
O	-1.32258000	1.20810200	0.49015700
C	-2.65806700	1.22096600	0.47820400
C	-3.24715800	2.08178200	-0.60349400
C	-4.29717700	2.98006200	-0.34251200
C	-4.78558300	3.83527100	-1.32939700
C	-4.21503800	3.79092400	-2.59655700
C	-3.16806700	2.92707200	-2.89600300
C	-2.68535300	2.08760700	-1.89145700
H	-1.85656600	1.42291600	-2.11048300
H	-2.74463000	2.92199000	-3.89552700
F	-4.68381800	4.61543200	-3.55953600
H	-5.59434400	4.53080200	-1.12893000
H	-4.73901600	3.00447200	0.64795200
C	-3.41436200	0.55961700	1.41648100
C	-2.71856800	-0.01183400	2.64459300
H	-1.74555000	-0.42500700	2.35457200
H	-3.30659300	-0.84544300	3.04835500
C	-2.47188100	1.02006900	3.76301900
H	-1.94413300	0.56646900	4.61153300
H	-1.86143200	1.84835500	3.38950600
H	-3.40891800	1.44446400	4.14033700
C	-4.87784500	0.33854600	1.30428800
C	-5.49302600	0.00380400	0.07857300
C	-6.85967300	-0.24885100	-0.01054800
C	-7.66617800	-0.19824200	1.12895600
C	-7.07851600	0.10530200	2.35733000
C	-5.71084500	0.36541300	2.44266800
H	-5.28400100	0.60471200	3.41174400
H	-7.68698200	0.14377900	3.25797900
H	-8.73141400	-0.40258500	1.06134400
H	-7.29440200	-0.50330500	-0.97442400
H	-4.88218100	-0.06429600	-0.81628000
N	-0.08603500	4.46936700	0.92228700
C	-0.40543100	5.00159400	-0.41398000
H	0.39529200	4.73111000	-1.11014000
H	-0.50315700	6.09848300	-0.42333100
H	-1.33985600	4.56113100	-0.77271900
C	-1.20780700	4.65041100	1.87866300
H	-0.91892100	4.13912300	2.80528700
H	-2.06474000	4.10577600	1.46864000
C	-1.62698400	6.09051100	2.20602500
H	-2.45375400	6.06696400	2.92453800
H	-0.81436500	6.66808300	2.65918900
H	-1.97821700	6.62947500	1.32023600
C	1.16995600	5.05315700	1.41910900
H	1.14170900	6.15332500	1.46177000
H	1.37977100	4.67267600	2.42358800
H	1.99197900	4.75737700	0.76133100
N	-0.46488100	-1.98518500	-0.64246400
C	-0.87275200	-2.74361600	0.55273200
H	-0.06453600	-2.71856200	1.29124100
H	-1.09304900	-3.79946500	0.33086000
H	-1.76215800	-2.28499400	0.99241600
C	-1.59121100	-1.81255100	-1.59683300
H	-1.22193700	-1.17506800	-2.40995300
H	-2.36538800	-1.24440400	-1.06919900
C	-2.20709300	-3.08441800	-2.19609200
H	-3.01016200	-2.80141100	-2.88537200
H	-1.47806400	-3.67230900	-2.76360000
H	-2.64715700	-3.72967200	-1.42927100
C	0.70677700	-2.61939600	-1.26802900
H	0.52241600	-3.66713400	-1.55270100
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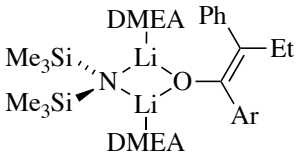

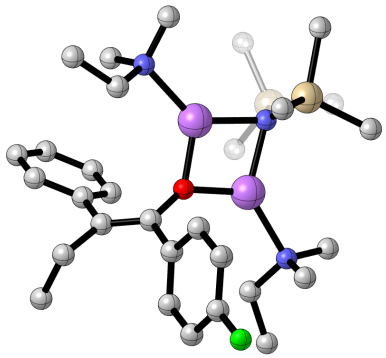

AZ(DMEA)$_2$
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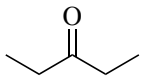
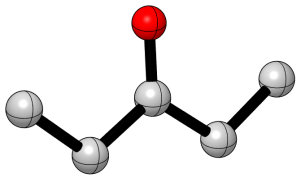
G_{MP2} = –1319248.026

Atom	X	Y	Z
Li	0.00000000	0.00000000	0.00000000
N	1.32970900	1.43291000	0.59306500
Si	2.36829900	0.92869300	1.88019700
C	3.39210700	-0.62860100	1.47270500
H	4.05886700	-0.46158800	0.61843600
H	4.01543700	-0.93287200	2.32380900
H	2.74550500	-1.48022000	1.22372600
C	1.33013800	0.46365800	3.41165400
H	1.98226500	0.14356600	4.23455100
H	0.73086600	1.30382100	3.78837200
H	0.64255600	-0.36350500	3.20027000
C	3.62421800	2.23733400	2.47310500
H	4.34842300	2.50570800	1.69400200
H	3.12879400	3.16321600	2.79047800
H	4.19637900	1.85926100	3.33048500
Si	1.91855400	2.33848000	-0.75622500
C	2.22168800	4.18768300	-0.39064600
H	1.29999600	4.69283300	-0.07221100
H	2.96697700	4.33318300	0.40013200
H	2.58341900	4.71230300	-1.28497100
C	0.63096800	2.32761700	-2.16538200
H	1.02857300	2.83400800	-3.05428200
H	0.34567600	1.31286800	-2.47511700
H	-0.28741800	2.85305600	-1.87621100
C	3.54575400	1.68675500	-1.50868300
H	4.37992300	1.74748100	-0.79884000
H	3.45918900	0.63869000	-1.82036800
H	3.82912800	2.27210800	-2.39325300
Li	-0.46603700	2.02826300	1.31506000
O	-1.59649000	0.67562600	0.70412400
C	-2.90915000	0.47589500	0.57650500
C	-3.62409000	1.63146000	-0.07334100
C	-4.71902200	2.27051700	0.53167900
C	-5.32889100	3.38372500	-0.05162700
C	-4.83230400	3.86021600	-1.25836100
C	-3.74817300	3.26017600	-1.89078700
C	-3.14853700	2.15596300	-1.28704900
H	-2.29655900	1.68600700	-1.76671700
H	-3.39121500	3.65688400	-2.83599500
F	-5.41499800	4.93624100	-1.83134400
H	-6.17300600	3.88086300	0.41583900
H	-5.09924600	1.89299300	1.47624500
C	-3.57902800	-0.66293100	0.95890200
C	-2.90633900	-1.75306900	1.71201500
C	-3.22628500	-3.11008700	1.49113200
C	-2.63029600	-4.13572000	2.22714400
C	-1.69652400	-3.84309000	3.22151100
C	-1.37503200	-2.50599000	3.47050700
C	-1.96762500	-1.48415700	2.73074800
H	-1.71581300	-0.45295800	2.94695400
H	-0.66490200	-2.25426500	4.25467000
H	-1.23629100	-4.63951200	3.80016000
H	-2.90194400	-5.16853400	2.02121500
H	-3.95159100	-3.37448000	0.72742900
C	-5.03818800	-0.90556400	0.59346200
H	-5.12114200	-1.83180200	0.00548000
H	-5.39385900	-0.11775700	-0.07432200
C	-5.99179700	-1.02205600	1.79583600
H	-7.01617300	-1.23315800	1.46506100
H	-5.68372100	-1.82647600	2.47227300
H	-6.01125000	-0.09349200	2.37924300
N	-1.07946100	3.70800100	2.47100300
C	-1.68106100	4.64461900	1.50511500
H	-0.94639700	4.88209300	0.72878100
H	-1.99478200	5.59220800	1.97062300
H	-2.54974500	4.18039700	1.03150600
C	-2.07607300	3.18467300	3.44023300
H	-1.55830700	2.43874400	4.05603600
H	-2.83090500	2.64614300	2.85757800
C	-2.76756300	4.20443900	4.35550700
H	-3.46694100	3.67816800	5.01456300
H	-2.05594700	4.73990800	4.99232300

H	-3.34267400	4.94328600	3.78798700
C	0.06974900	4.33922600	3.13953600
H	-0.20163300	5.26896600	3.66423500
H	0.50286000	3.64397400	3.86463300
H	0.83394400	4.57726800	2.39464800
N	0.12804200	-1.73574100	-1.22130400
C	0.20366600	-2.87917100	-0.29373900
H	1.08989100	-2.77053900	0.33933400
H	0.28341800	-3.84350100	-0.81984500
H	-0.68160200	-2.89872500	0.34556800
C	-1.14479900	-1.72199400	-1.98845800
H	-1.13023200	-0.81493200	-2.60639200
H	-1.95421900	-1.59800800	-1.26092500
C	-1.44034100	-2.93390900	-2.88298400
H	-2.39364300	-2.77271300	-3.39859700
H	-0.67343500	-3.08476300	-3.65023300
H	-1.53302500	-3.85857800	-2.30436700
C	1.30827000	-1.72170700	-2.09938600
H	1.41199500	-2.64714400	-2.68791400
H	1.24767900	-0.87554000	-2.79046300
H	2.20877300	-1.60382900	-1.48979500

Table A.1.6. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant ground states of LiHMDS/DMEA-mediated enolization of 3-pentanone at –40 °C with free energies (Hartrees), corrected MP2 energies (kcal) and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)



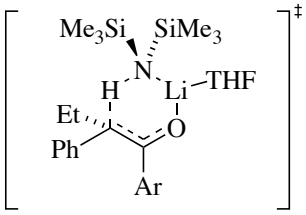


3-pentanone
G = –271.667264
G_{MP2} = –169891.480

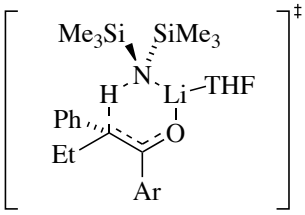
Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
H	0.36944100	0.05245400	1.03607400
H	0.78366900	0.39304900	-0.65835500
C	-0.43145400	-1.42747100	-0.35907500
H	-0.36819400	-1.58569300	-1.44243900
H	0.17898100	-2.19202000	0.13156300
C	-1.89873200	-1.42780000	0.09478400
H	-2.50889400	-2.19240900	-0.39610500
H	-1.96191900	-1.58645800	1.17808700
C	-2.33082600	-0.00036200	-0.26378100
H	-2.70107000	0.05220800	-1.29954200
H	-3.11413200	0.39228800	0.39526100
O	-1.16547600	0.82075200	-0.13234900

V: Transition State Computations

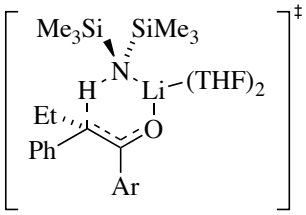
Chart A.1.2



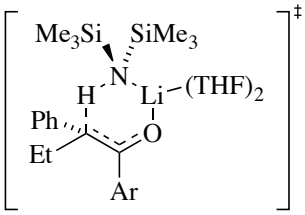
A(ketone)(THF) - Pro E



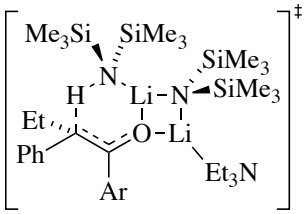
A_2(ketone)(THF) - Pro Z



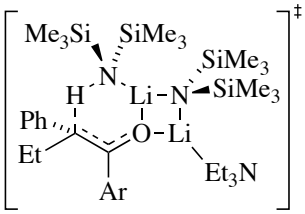
A(ketone)$(THF)_2$ - Pro E



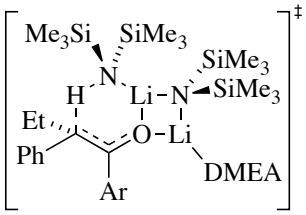
A_2(ketone)$(THF)_2$ - Pro Z



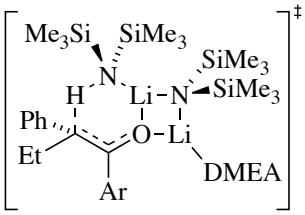
A_2(ketone)(Et_3N) - Pro E



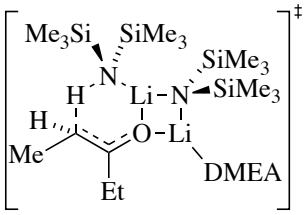
A_2(ketone)(Et_3N) - Pro Z



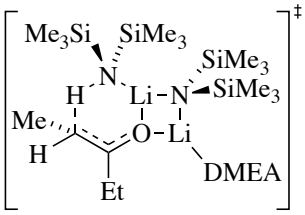
A_2(ketone)(DMEA) - Pro E



A_2(ketone)(DMEA) - Pro Z

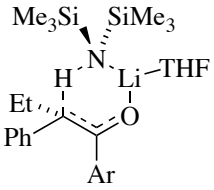


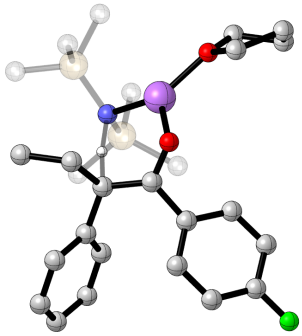
A_2(3-pentanone)(DMEA) - Pro E



A_2(3-pentanone)(DMEA) - Pro Z

Table A.1.7. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for transition states of LiHMDS/THF-mediated enolizations of 1-(4-fluorophenyl)-2-butan-1-one (ketone) at 0 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

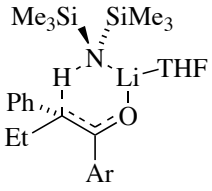


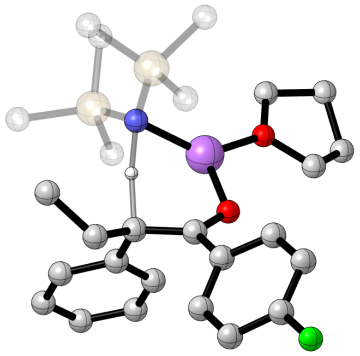


A(ketone)(THF)
Pro E
G = –1906.613695
G_{MP2} = –1193007.586

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
Li	-1.32550500	2.58027100	-0.06487000
O	-2.93048400	2.98136500	-0.87063600
C	-3.94871400	2.31517900	-0.50663300
C	-5.08581100	3.14950000	0.02187400
C	-6.43453300	2.85756500	-0.24247500
C	-7.44905700	3.72797200	0.15047500
C	-7.10827800	4.89043600	0.83144000
C	-5.78581900	5.21872800	1.11037700
C	-4.78390100	4.35213100	0.68463300
H	-3.74430400	4.60167200	0.86673000
H	-5.56148700	6.13844500	1.64098200
F	-8.08719600	5.72868000	1.22948400
H	-8.49186100	3.51481200	-0.06005300
H	-6.69949000	1.94902900	-0.76835300
C	-3.93565100	0.85697700	-0.57379100
C	-5.11926200	0.12119500	0.00719300
C	-6.00482600	-0.63663500	-0.78575100
C	-7.10606300	-1.29406900	-0.23490600
C	-7.36556500	-1.21603700	1.13368000
C	-6.50737800	-0.46698000	1.93946000
C	-5.40620100	0.18333500	1.38315000
H	-4.75918800	0.76313200	2.03059700
H	-6.69066500	-0.38921000	3.00836600
H	-8.22058100	-1.73029300	1.56437100
H	-7.76622500	-1.86554800	-0.88328300
H	-5.85096800	-0.69858200	-1.85807700
C	-3.45741500	0.33237600	-1.95143800
H	-2.59952500	0.93376800	-2.25777400
H	-4.23381700	0.52545600	-2.70930000
C	-3.08593400	-1.15522700	-2.00062900
H	-2.66853100	-1.41171500	-2.98213400
H	-2.34231200	-1.40720100	-1.24132400
H	-3.94808200	-1.80518500	-1.83086100
N	-1.39810900	0.76051800	0.75437400
Si	-1.61228200	0.70948900	2.49901700
C	-2.46044200	-0.88102100	3.09190900
H	-1.78812400	-1.73720200	2.95443600
H	-2.70288900	-0.82436300	4.16127000
H	-3.38366000	-1.10031200	2.54835400
C	-0.00974600	0.81155300	3.52481400
H	0.61075900	1.68048400	3.27668300
H	-0.28704400	0.89875200	4.58409400
H	0.61594900	-0.08286700	3.43032100
C	-2.59702100	2.24359500	3.05454300
H	-3.51954400	2.42031200	2.49375200
H	-2.86632900	2.16795200	4.11587000
H	-1.97665400	3.14555000	2.94867900
O	-0.17256600	4.12001200	-0.09904800
C	0.60085600	4.67573300	0.98610000
H	1.67084500	4.54011600	0.77832100
H	0.34532400	4.12162300	1.89298300
C	0.21563700	6.15166500	1.01689100
H	-0.74249300	6.28096300	1.53342700
H	0.96318400	6.77155900	1.52028600
C	0.07492000	6.47011800	-0.48175700

H	-0.58172700	7.32237700	-0.67740300
H	1.05605700	6.69679700	-0.91340400
C	-0.48563600	5.16439900	-1.06813700
H	-1.57212900	5.17233200	-1.18650200
H	-0.02656800	4.89684400	-2.02495300
C	0.12119800	-1.87794900	0.26676700
H	0.27284900	-2.11319400	1.32773600
H	-0.77636900	-2.41379700	-0.06017500
H	0.97577700	-2.29271200	-0.28348400
C	1.65937400	0.72711000	0.60269400
H	1.68151100	1.82063000	0.50736600
H	1.90655900	0.47830400	1.63786800
H	2.46604800	0.33358700	-0.03008800
C	0.06422100	0.36510400	-1.87018600
H	-0.07900500	1.43095300	-2.09761200
H	1.06485600	0.09992000	-2.23559900
H	-0.65951100	-0.19772400	-2.46332100
H	-2.68463000	0.68591800	0.17149600

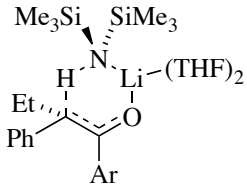


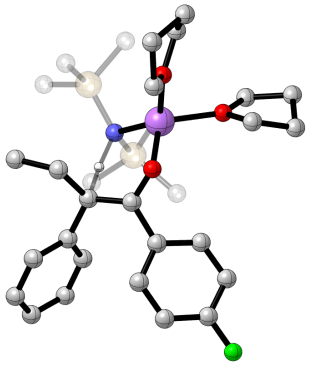


A(ketone)(THF)
Pro Z
G = –1906.621065
G_{MP2} = –1193012.043

Atom	**X**	**Y**	**Z**
C	0.00000000	0.00000000	0.00000000
C	0.75993400	0.99703400	0.90634600
C	0.16962300	2.33414000	1.05671000
C	-1.26647800	2.66149700	0.77026500
C	-2.30333900	1.77585000	1.10703800
C	-3.63888700	2.14407000	0.95980100
C	-3.92954600	3.40728500	0.45695500
C	-2.93128300	4.31615000	0.11938100
C	-1.60358100	3.94024100	0.29608900
H	-0.80768500	4.64027600	0.06662600
H	-3.20401500	5.29422100	-0.26345900
F	-5.21910200	3.76644800	0.29856700
H	-4.44847200	1.47392800	1.22932200
H	-2.06532500	0.79813900	1.51163300
O	0.87584500	3.30657000	1.44769800
Li	2.72382300	3.30072000	1.13460600
N	3.14551900	1.93274100	-0.25360900
Si	4.62267900	1.11421100	0.22593200
C	4.65044200	-0.73619900	-0.19577500
H	4.45635200	-0.91390200	-1.26001800
H	5.62922100	-1.17316400	0.04153700
H	3.89765300	-1.28575400	0.38012900
C	6.18501900	1.88048200	-0.55723500
H	6.31357300	2.93155100	-0.27018500
H	7.07019000	1.33698600	-0.20121900
H	6.19589700	1.83408700	-1.65158600
C	4.90060600	1.27382800	2.10074500
H	4.13142700	0.76507200	2.68866000
H	5.86874700	0.82859400	2.36585900
H	4.93530100	2.32180800	2.43204600
Si	2.95549400	2.60529400	-1.86006200
C	3.53231000	1.46811900	-3.27380700
H	4.59894800	1.22423300	-3.21210000
H	2.98108000	0.52033000	-3.28342900
H	3.36505000	1.95489700	-4.24360300
C	3.89073600	4.25703700	-2.04767000
H	3.57857800	4.97445100	-1.27609900
H	4.97705800	4.13667100	-1.97129500
H	3.67733700	4.71516500	-3.02243300
C	1.13770200	3.02798400	-2.21192500
H	0.75982800	3.79999200	-1.53240900
H	1.04851500	3.42194200	-3.23248500
H	0.46847200	2.16444600	-2.13618300
O	3.49461900	4.90105800	1.86752600
C	2.66276400	5.83337200	2.60817300
H	2.00781600	5.25316300	3.26119000

H	2.04337900	6.38981000	1.89419200
C	3.64304000	6.74618200	3.34129700
H	3.20988400	7.72477900	3.56754400
H	3.96273600	6.28733300	4.28421100
C	4.81621500	6.81535000	2.35072900
H	4.59761800	7.53049100	1.54926300
H	5.76154900	7.10691900	2.81711600
C	4.85932000	5.38857800	1.79866300
H	5.19173000	5.32813300	0.75893200
H	5.48949100	4.73310400	2.41139100
C	1.28627500	0.40724400	2.20004800
C	1.58823700	-0.96849100	2.28221400
C	2.04600800	-1.55636000	3.46272600
C	2.21463800	-0.79603900	4.61859200
C	1.90978200	0.56512700	4.56716300
C	1.46172800	1.15471700	3.38574400
H	1.22350300	2.21238200	3.39416700
H	2.01469400	1.18054200	5.45805900
H	2.56977500	-1.25257300	5.53835500
H	2.26700200	-2.62117900	3.47217000
H	1.45776600	-1.60216400	1.41368700
H	-0.77015200	0.54367500	-0.55602600
H	-0.53674100	-0.74500100	0.60637200
C	0.84522700	-0.74684300	-1.04812800
H	0.21065800	-1.44174400	-1.61211900
H	1.29417600	-0.05162800	-1.76223700
H	1.66289400	-1.32557900	-0.61007100
H	1.96145400	1.38582800	0.24750500

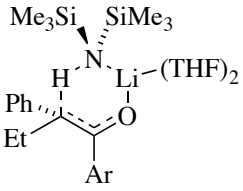


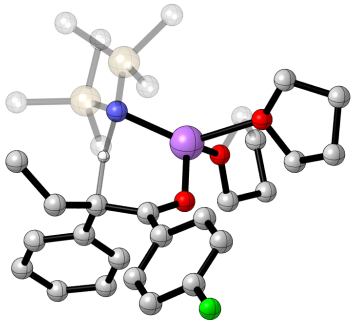


A(ketone)(THF)$_2$
Pro E
G = –2138.962624
G_{MP2} = –1338329.494

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	-0.61478000	0.65436600	1.26273000
C	-0.32802700	2.08189700	1.37640500
C	-1.34158400	3.13341400	1.75843200
C	-2.63394300	3.18111200	1.21115500
C	-3.49067900	4.24759900	1.47931800
C	-3.05345500	5.26302700	2.32045200
C	-1.78205700	5.25382500	2.88383100
C	-0.92982300	4.19594200	2.58088700
H	0.07163600	4.17594700	2.99511800
H	-1.47858400	6.06580500	3.53696200
F	-3.88411200	6.29051600	2.59733800
H	-4.48643100	4.29623800	1.05096200
H	-2.97763100	2.38531900	0.56237700
O	0.84566400	2.51983500	1.20169200
Li	2.33941800	1.84557200	2.13834700
O	3.73653100	2.22138900	0.61838500
C	3.30741300	2.68529600	-0.68589300
H	2.92388800	3.70768900	-0.58490700
H	2.49026700	2.04439700	-1.02056600
C	4.55497400	2.62929700	-1.56786600
H	4.68311200	1.62497500	-1.98836600
H	4.51238900	3.34255400	-2.39645100
C	5.67318500	2.93291200	-0.55887000
H	6.65928800	2.58630900	-0.88192000
H	5.73656600	4.01204800	-0.37360700
C	5.17733800	2.20015300	0.69106700
H	5.51213700	1.15548900	0.70611300
H	5.48040800	2.67691500	1.62860500
O	3.16716200	3.32606500	3.30491800
C	3.14506000	4.64716700	2.72066600
H	2.19160100	4.75971600	2.20097000

H	3.95772800	4.73245100	1.98599300
C	3.35797400	5.59915100	3.89416000
H	3.74122200	6.57524500	3.58207000
H	2.41660700	5.75593100	4.43373600
C	4.34991400	4.80330800	4.75787200
H	5.36866300	4.92177800	4.37024600
H	4.35329000	5.10764900	5.80846200
C	3.86396700	3.35887400	4.57426800
H	4.67782100	2.62715500	4.54825600
H	3.15735000	3.06335800	5.35641400
C	-2.02721500	0.21053100	1.57016700
C	-2.90680300	-0.24654700	0.56710900
C	-4.21717900	-0.62951200	0.85524000
C	-4.70061400	-0.56698600	2.16307500
C	-3.85286900	-0.11097400	3.17238300
C	-2.54243400	0.26632500	2.87668600
H	-1.90661700	0.61974400	3.67866200
H	-4.20791000	-0.05040500	4.19830800
H	-5.71981200	-0.86825700	2.39031500
H	-4.86352600	-0.97295700	0.05070400
H	-2.57300700	-0.28212600	-0.46540100
H	1.04589800	0.30825200	-0.06218400
H	-0.48153000	0.39912400	-0.90774900
C	-0.07704800	-1.53300600	-0.03596500
H	0.46972300	-1.92242500	-0.90319600
H	0.35673800	-1.97514900	0.86541100
H	-1.10499200	-1.89584400	-0.10730000
H	0.41312500	0.23698700	2.19110400
C	-0.17508100	-1.29867100	5.06280800
H	0.33429400	-2.26829200	5.11480200
H	-0.63694000	-1.11994300	6.04307700
H	-0.97886900	-1.39169400	4.32676200
Si	1.06323800	0.08155200	4.63568600
C	2.43994100	-0.11626200	5.94383800
H	3.25532600	0.60762700	5.83634500
H	1.99360600	0.03688200	6.93592100
H	2.88337200	-1.11817000	5.94569200
C	0.28376800	1.76878600	5.04458000
H	-0.59629800	2.01588400	4.44466900
H	-0.01957600	1.79751900	6.09926100
H	1.01287200	2.57234400	4.88599500
N	1.59653300	0.03890400	2.95986900
Si	2.83679200	-1.13213000	2.52596500
C	2.44852400	-2.93046300	3.01747500
H	2.41873200	-3.06950500	4.10470800
H	1.48251800	-3.26177900	2.61816000
H	3.21850800	-3.60683300	2.62346000
C	4.52478500	-0.70158400	3.31962400
H	4.81244900	0.33807600	3.11213700
H	4.54871100	-0.83530900	4.40442800
H	5.30647100	-1.34410700	2.89252100
C	3.26000700	-1.16202600	0.67049900
H	3.43816800	-0.15464700	0.28086800
H	4.19008700	-1.73358900	0.54933800
H	2.50222400	-1.64150500	0.04807800



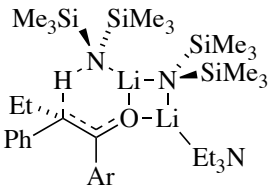


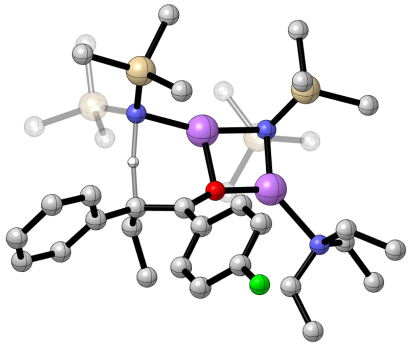
A(ketone)(THF)$_2$
Pro Z
G = –2138.965538
G_{MP2} = –1338330.678

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	-0.71891900	1.01807500	-0.91908800
C	0.05818700	2.20760000	-1.28999400
C	1.55621100	2.29602700	-1.18323700
C	2.38164900	1.23163000	-1.57935500
C	3.76821200	1.36824100	-1.60353300

C	4.32463700	2.57962500	-1.20886600
C	3.54041200	3.65870200	-0.81323800
C	2.15628800	3.51226500	-0.82135700
H	1.52008700	4.34434800	-0.54007200
H	4.01818600	4.58647400	-0.51517300
F	5.66643400	2.71587300	-1.21466100
H	4.41597000	0.55770200	-1.92086400
H	1.93488200	0.29375900	-1.89201000
O	-0.51020700	3.24527700	-1.72358000
Li	-2.16849900	3.92272500	-1.03735100
O	-1.33246000	6.01375400	-0.75347600
C	-0.67749600	6.41240100	-1.97991900
H	-1.41286000	6.90025500	-2.63566000
H	-0.30579700	5.50686300	-2.46147800
C	0.41872600	7.39102700	-1.56235300
H	1.31846400	6.84652700	-1.25225400
H	0.69869700	8.07714100	-2.36751400
C	-0.23008800	8.09214300	-0.36014000
H	0.49243700	8.55309400	0.31997800
H	-0.91738200	8.87500200	-0.70260700
C	-1.00415900	6.94728100	0.30258100
H	-0.39569400	6.42625300	1.05103700
H	-1.93024200	7.27524800	0.78311400
O	-3.34190000	4.68307900	-2.47618900
C	-4.35658700	5.67781700	-2.21565500
H	-3.86128400	6.60827500	-1.91088500
H	-4.97806600	5.32283700	-1.38821800
C	-5.12266900	5.84052400	-3.53020900
H	-5.92786000	5.10020700	-3.59736100
H	-5.56514300	6.83562700	-3.63468700
C	-4.03490200	5.54320300	-4.57448400
H	-4.43774700	5.23619600	-5.54406500
H	-3.40490200	6.42681600	-4.73249700
C	-3.23648400	4.42730500	-3.89705200
H	-3.65737900	3.43677900	-4.10262600
H	-2.17557200	4.42110200	-4.16153500
C	-1.46923700	0.38929800	-2.07718500
C	-1.97411700	-0.92332700	-1.96878500
C	-2.63019400	-1.55409700	-3.02768900
C	-2.80119900	-0.90395800	-4.24814600
C	-2.29974800	0.39198000	-4.38411900
C	-1.65633100	1.02651500	-3.32275800
H	-1.27709200	2.03059600	-3.46965900
H	-2.40256500	0.91782400	-5.33135400
H	-3.30839700	-1.39459200	-5.07444300
H	-3.00411600	-2.56611400	-2.89042300
H	-1.85062100	-1.47584400	-1.04534100
H	0.90932800	0.46165300	0.39702200
H	0.33722600	-0.87128500	-0.58117400
C	-0.79198600	-0.50694600	1.21702600
H	-0.19946200	-1.25075900	1.76447900
H	-1.01755000	0.30978600	1.90645600
H	-1.74472800	-0.97168000	0.95026600
H	-1.74435300	1.68315900	-0.20254000
C	-4.55864500	0.02729700	0.80674000
H	-4.24925900	-0.06132200	1.85408900
H	-5.60699500	-0.29322800	0.74121000
H	-3.96550300	-0.68141000	0.21836900
Si	-4.37386700	1.79836400	0.13726700
C	-5.73697000	2.82445100	0.99792700
H	-5.73281800	3.87474100	0.68045000
H	-6.71859400	2.40722500	0.73674100
H	-5.66237400	2.81245100	2.09123400
C	-4.90504900	1.72988800	-1.68238800
H	-4.25007800	1.09848100	-2.28879000
H	-5.91985700	1.31467400	-1.74448900
H	-4.92423800	2.72733100	-2.13437100
N	-2.76750400	2.47966800	0.36250300
Si	-2.34577900	3.14256800	1.92762300
C	-2.79527700	2.08617500	3.44995400
H	-3.87686500	1.92771000	3.53453800
H	-2.31986800	1.09945400	3.44479800
H	-2.47181400	2.60227100	4.36404900
C	-3.18958300	4.82651700	2.24775200
H	-3.19861200	5.45947500	1.35315800
H	-4.22968200	4.69955000	2.56607000
H	-2.66889400	5.37817400	3.04208300
C	-0.47045200	3.44623600	2.00865600
H	-0.13596600	4.11737200	1.20955800
H	-0.20335600	3.91023200	2.96685000
H	0.10803500	2.51975400	1.92131700

Table A.1.8. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for transition states of LiHMDS/Et_3N-mediated enolizations of 1-(4-fluorophenyl)-2-butan-1-one (ketone) at 0 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

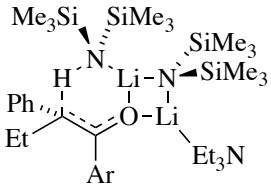


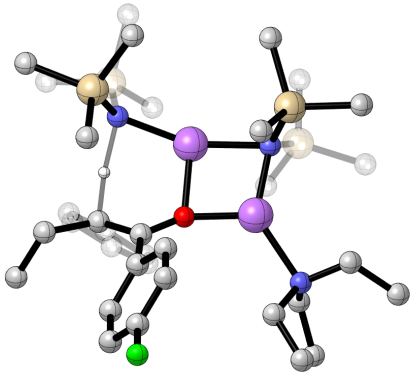


A_2(ketone)(Et_3N)
Pro E
G = –2847.219263
G_{MP2} = –1781691.169

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	1.77130400	0.44639600	-0.53198500
H	2.46593000	0.43308100	0.31560500
H	2.14273700	-0.27190700	-1.27488500
H	1.82934500	1.44594500	-0.97879400
C	0.08479500	-1.73764000	0.77708000
H	0.72241900	-1.78237200	1.66656500
H	-0.90828100	-2.10807500	1.05880000
H	0.50114500	-2.44012500	0.04323500
N	-0.70615200	1.21032800	1.06732200
Si	-0.26518800	1.15446200	2.76650300
C	-1.15578000	-0.24589400	3.70209700
H	-2.24501200	-0.18045800	3.58525800
H	-0.85232100	-1.24189800	3.36615700
H	-0.93930000	-0.17890700	4.77673500
C	-0.80763100	2.73582700	3.67869900
H	-0.70567700	2.56770500	4.75875900
H	-0.20708200	3.61740000	3.43590000
H	-1.85590600	2.98940000	3.49471000
C	1.59811600	0.97945800	3.11288500
H	2.00487700	0.02009100	2.77355900
H	2.17152400	1.77435700	2.62129000
H	1.78740200	1.05014300	4.19212000
Li	-2.70523400	1.67896000	0.99066100
N	-4.78790000	1.51565000	1.02179800
Si	-5.28943200	0.55394500	-0.33561100
C	-4.62221600	-1.23007900	-0.29700500
H	-5.13976400	-1.82262400	0.46677800
H	-4.77187800	-1.73434800	-1.26067100
H	-3.55212400	-1.27275600	-0.06336800
C	-4.66325000	1.36393700	-1.94859300
H	-5.00705100	0.79163300	-2.81974800
H	-5.04105200	2.38896100	-2.07459800
H	-3.56995800	1.40771600	-2.00952000
C	-7.17380000	0.36562500	-0.57445900
H	-7.64047800	-0.19838900	0.24200000
H	-7.69133500	1.33001800	-0.64539700
H	-7.37627200	-0.18522700	-1.50264000
Si	-5.52949800	1.28155700	2.57494700
C	-7.33965700	1.88720000	2.69106000
H	-7.42512800	2.96946000	2.52579600
H	-7.99953800	1.39311400	1.96996500
H	-7.73969000	1.68618400	3.69395300
C	-4.61578400	2.28311300	3.91385700
H	-5.19425700	2.27882700	4.84667200
H	-3.62962000	1.86740000	4.14598300
H	-4.47404900	3.33532900	3.62962300
C	-5.55904700	-0.52380200	3.18016000
H	-6.22206200	-1.14972300	2.57036900
H	-4.56263600	-0.98139700	3.15419500
H	-5.92219600	-0.57868800	4.21476500
Li	-4.57222000	3.43967700	0.55392900
O	-2.69970500	3.70875600	0.66390000
C	-1.59553300	4.34646200	0.57127000

C	-1.52469100	5.65464200	1.28544400
C	-0.81885300	6.74839200	0.75177000
C	-0.85974800	7.99625700	1.36764100
C	-1.59518800	8.14078700	2.53951200
C	-2.30295800	7.08263100	3.10217500
C	-2.27500800	5.84841000	2.45963500
H	-2.82284700	5.01292400	2.88007900
H	-2.85628900	7.23515800	4.02304200
F	-1.62521600	9.34109700	3.14741000
H	-0.32848400	8.84913600	0.95868600
H	-0.24056100	6.62635200	-0.15615000
C	-0.50963600	3.73514300	-0.18422300
C	-0.98519200	3.24335700	-1.57377700
H	-1.77143300	2.49947900	-1.43410000
H	-0.15664800	2.71289400	-2.05256000
C	-1.52014500	4.33565100	-2.51360600
H	-1.78911200	3.90733800	-3.48677000
H	-2.42137700	4.80137700	-2.09916700
H	-0.78960800	5.13188100	-2.69072900
C	0.88424600	4.31515900	-0.13415300
C	1.51731700	4.53887100	1.10384600
C	2.82074200	5.02274500	1.18754000
C	3.55124800	5.28604200	0.02702300
C	2.95580600	5.05025400	-1.21067800
C	1.64598800	4.57066000	-1.28970000
H	1.22331500	4.39592900	-2.27252200
H	3.50980100	5.23752800	-2.12723400
H	4.57073200	5.65685700	0.08804400
H	3.27001100	5.18245900	2.16448800
H	0.97767600	4.32596700	2.01911700
N	-5.86494100	5.09602400	0.08711000
C	-6.00935800	5.68017500	1.44176700
H	-6.08638800	4.84462900	2.15178200
H	-5.06399800	6.18797000	1.66387300
C	-7.18237300	6.62978400	1.73169800
H	-7.18993600	7.50787700	1.08078500
H	-8.14635400	6.12076100	1.63429300
H	-7.10417400	6.97997400	2.76798500
C	-5.08421200	5.91211000	-0.87140100
H	-5.12354900	5.38471300	-1.83270400
H	-4.03811700	5.88189400	-0.54279400
C	-5.46006300	7.38783900	-1.08280900
H	-4.80207300	7.81244100	-1.85049200
H	-6.49284700	7.52292400	-1.41373700
H	-5.31186100	7.97405500	-0.17046600
C	-7.08066600	4.45411000	-0.46754500
H	-6.74483100	3.65942300	-1.14584900
H	-7.57486100	3.94712500	0.36776600
C	-8.10445800	5.31042000	-1.22938100
H	-7.67994400	5.72808800	-2.14798000
H	-8.94555500	4.67121800	-1.52347600
H	-8.50302000	6.13338200	-0.63077500
C	-0.98341100	-0.26125500	-1.60924500
H	-2.05609300	-0.39823600	-1.43922900
H	-0.85748400	0.54990600	-2.33204500
H	-0.61809100	-1.17841000	-2.08994000
H	-0.47988600	2.58032300	0.46671200





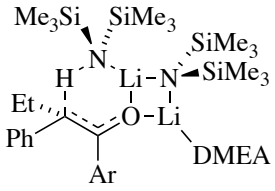
A_2(ketone)(Et_3N)
Pro Z
G = –2847.21147
G_{MP2} = –1781687.453

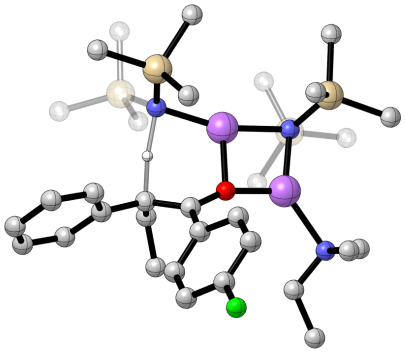
Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	-1.58246100	0.79122700	0.70637500
H	-2.16539100	1.31944600	-0.05470300
H	-2.22281100	-0.00020000	1.11876600

H	-1.37757300	1.49412000	1.51899400
C	-0.62034000	-1.40012600	-1.13582600
H	-1.27272300	-1.04410400	-1.94145000
H	0.20552900	-1.95330600	-1.59851400
H	-1.20295700	-2.11669000	-0.54150100
N	1.13133100	1.08401000	-0.80244900
Si	0.66859900	1.67920800	-2.39020200
C	0.88169900	0.41473000	-3.79701000
H	1.92720400	0.10760800	-3.91353000
H	0.28499400	-0.49247000	-3.66109500
H	0.57047400	0.87347300	-4.74545600
C	1.71077900	3.16317600	-2.96081800
H	1.34183800	3.47307500	-3.94728600
H	1.63908400	4.03468900	-2.30331300
H	2.77032800	2.91866600	-3.08313100
C	-1.13525400	2.29079100	-2.49616700
H	-1.86716500	1.48115500	-2.39459000
H	-1.36024700	3.03778800	-1.72501100
H	-1.30883900	2.76266100	-3.47216600
Li	2.99915400	0.23434600	-0.39615300
N	4.66195500	-1.08232300	-0.54248900
Si	4.80229100	-2.29614500	0.69476700
C	3.62895800	-3.78306700	0.47457100
H	3.93589400	-4.40770800	-0.37386900
H	3.64147100	-4.42198100	1.36726000
H	2.58990900	-3.48274800	0.29683400
C	4.47034800	-1.54221900	2.41161500
H	5.17004200	-0.72892100	2.64433100
H	3.45912300	-1.14081300	2.52371000
H	4.60548400	-2.30908000	3.18567400
C	6.53378300	-3.09154700	0.87270200
H	6.87884800	-3.57524500	-0.04728000
H	7.30446100	-2.36914900	1.17108100
H	6.50148600	-3.86211300	1.65476900
Si	4.83796600	-1.49063000	-2.21992000
C	6.35098000	-2.55904400	-2.67932400
H	7.29593600	-2.13553400	-2.31779800
H	6.27199700	-3.57716200	-2.28052900
H	6.42563800	-2.64526600	-3.77155500
C	5.05356800	0.12463100	-3.21985300
H	5.15341000	-0.08934500	-4.29137200
H	4.19901000	0.80333800	-3.10709800
H	5.96050100	0.66986100	-2.91882100
C	3.34246900	-2.41398300	-2.94760100
H	3.27663600	-3.43138300	-2.54408600
H	2.39715400	-1.91055700	-2.71775900
H	3.41448800	-2.49795900	-4.03992900
Li	5.59110700	0.61300200	-0.08355400
O	4.14453600	1.83715000	0.09602200
C	3.61449800	2.99676000	0.14407200
C	4.35644800	4.08068500	-0.57359300
C	4.53765100	5.35193400	-0.00551000
C	5.31425000	6.32122500	-0.63739500
C	5.89506600	6.01572100	-1.86301400
C	5.74240000	4.76705000	-2.45850100
C	4.98972800	3.80128900	-1.79746200
H	4.87701400	2.81939400	-2.24207800
H	6.20904200	4.56797200	-3.41771300
F	6.63270700	6.95148900	-2.48839300
H	5.47008000	7.30059600	-0.19745300
H	4.09048300	5.58152900	0.95335000
C	2.30557400	3.15897700	0.76866300
C	2.14134200	2.58753000	2.16830000
C	0.86648800	2.58372400	2.76122700
C	0.66522100	2.12727700	4.06363500
C	1.73897200	1.65409000	4.81788800
C	3.01266800	1.65119800	4.24888700
C	3.20957700	2.11268700	2.94652200
H	4.21151900	2.09579600	2.53224500
H	3.86400700	1.29022700	4.82035900
H	1.58631600	1.29450300	5.83166000
H	-0.33671900	2.13893200	4.48499000
H	0.01625700	2.94961200	2.19640500
C	1.52280200	4.47606800	0.53295100
H	0.48694900	4.20499700	0.28671200
H	1.90823500	4.95135400	-0.37334200
C	1.47203300	5.52023300	1.66256100
H	0.97120600	6.42767100	1.30512600
H	0.92005200	5.15663800	2.53263100
H	2.46536700	5.81017100	2.02157200
N	7.63520800	1.15123400	0.43997200
C	7.81315400	2.56289900	0.03282300
H	7.36151900	2.67238800	-0.96017300
H	7.19814000	3.16654700	0.71030400
C	9.23033800	3.15471500	-0.04069400
H	9.76657400	3.10577000	0.91019800
H	9.83720700	2.65404700	-0.80188900
H	9.15366200	4.20963900	-0.32993300
C	7.55712100	0.91935800	1.90065200
H	7.50364900	-0.16526900	2.04389600
H	6.59184300	1.32210100	2.24128800
C	8.64161800	1.50198900	2.82150000

H	8.43346400	1.18789500	3.85136100
H	9.64646300	1.15904100	2.56296900
H	8.63720900	2.59637400	2.80903000
C	8.44396000	0.17081500	-0.32516800
H	7.87603100	-0.76564600	-0.35734700
H	8.48147600	0.54097500	-1.35721700
C	9.86648600	-0.16178800	0.15092400
H	9.85860100	-0.64435800	1.13364800
H	10.3154920	-0.87236000	-0.55314100
H	10.5168980	0.71513900	0.20436100
C	0.85411100	-0.88356900	1.44632800
H	1.64173400	-1.56611900	1.10618200
H	1.28764200	-0.19005200	2.17346600
H	0.12004500	-1.49992400	1.98175800
H	1.69410900	2.24853600	0.03122600

Table A.1.9. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for transition states of LiHMDS/DMEA-mediated enolizations of 1-(4-fluorophenyl)-2-butan-1-one (ketone) at 0 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

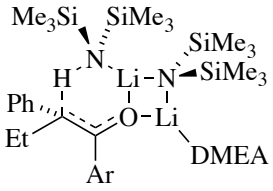


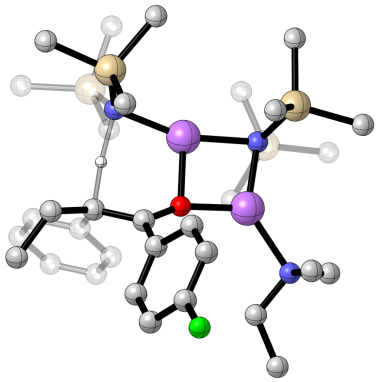


A_2(ketone)(DMEA)
Pro E
G = –2768.63968
G_{MP2} = –1732565.241

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	1.80308200	-0.30280000	-0.52651000
H	2.42835200	-0.60177500	0.32256900
H	1.85479900	-1.10653600	-1.27300100
H	2.26527300	0.58862600	-0.96634300
C	-0.62406400	-1.63732500	0.75057300
H	-0.07119200	-1.94774900	1.64405700
H	-1.68694200	-1.58788400	1.01656500
H	-0.51017500	-2.43608900	0.00584600
N	-0.16559100	1.38182200	1.07863800
Si	0.17866400	1.12902400	2.78283100
C	-1.23665800	0.21200300	3.66884200
H	-2.19671200	0.72507700	3.52941700
H	-1.36340200	-0.81523300	3.31416000
H	-1.04473900	0.16845500	4.74929300
C	0.33127000	2.78365200	3.71576600
H	0.22483900	2.59308200	4.79151100
H	1.30253000	3.26737800	3.57457600
H	-0.44361500	3.50540600	3.44162900
C	1.79484500	0.19482700	3.14969700
H	1.77229500	-0.84704100	2.81084300
H	2.65073800	0.68282200	2.66820800
H	1.98412600	0.18224900	4.23126200
C	-1.00227300	0.17210700	-1.60931000
H	-2.05225500	0.42700700	-1.43164300
H	-0.59054400	0.90811400	-2.30594000
H	-0.99300200	-0.79719800	-2.12511400
Li	-1.80186400	2.61318200	0.98420000
N	-3.76337500	3.31837200	1.00612200
Si	-4.61406200	2.66698800	-0.36059800
C	-4.75915500	0.76814300	-0.33784600
H	-5.47358000	0.44306200	0.42796400
H	-5.11306400	0.38127300	-1.30242100
H	-3.80561600	0.27611700	-0.11368500
C	-3.69251900	3.16154900	-1.95950800
H	-4.21086100	2.76587300	-2.84226400
H	-3.64615700	4.25360700	-2.08244300
H	-2.66483400	2.78209200	-1.99799300
C	-6.39917700	3.29513500	-0.60481900
H	-7.06402600	2.97675300	0.20676600
H	-6.45445100	4.38879200	-0.66598500
H	-6.81318400	2.89154600	-1.53836100
Si	-4.54379600	3.43194500	2.55290100
C	-5.90830100	4.76826700	2.64776200
H	-5.50529200	5.77604300	2.47705000
H	-6.71150800	4.60868100	1.92025800
H	-6.36551100	4.77401000	3.64619000
C	-3.29782100	3.95154000	3.89647700
H	-3.82444200	4.17015500	4.83438000
H	-2.56173400	3.17107000	4.11549700
H	-2.74489000	4.86093700	3.62139000
C	-5.35806300	1.81921400	3.15424900
H	-6.22731600	1.54608800	2.54304600
H	-4.65954700	0.97409500	3.12551300

H	-5.70958800	1.92417500	4.18896000
Li	-2.78125600	4.98068700	0.54129700
O	-0.96680700	4.46991200	0.67432400
C	0.30024500	4.61768500	0.60608100
C	0.86615200	5.80732900	1.30711700
C	1.95560400	6.52126400	0.77573000
C	2.39799100	7.69943200	1.37071700
C	1.75690200	8.15026800	2.52016000
C	0.67906800	7.47016300	3.07994600
C	0.23057600	6.30867400	2.45755400
H	-0.61082300	5.76665000	2.87435700
H	0.21352400	7.85124600	3.98300900
F	2.19055600	9.28007700	3.10862300
H	3.23006200	8.26408400	0.96364400
H	2.45592600	6.15710400	-0.11358200
C	1.07150900	3.61690500	-0.12190800
C	0.48705000	3.37462800	-1.53571900
H	-0.55329700	3.06030500	-1.43513200
H	1.01166200	2.52794900	-1.98808000
C	0.53542500	4.58594500	-2.48093800
H	0.14331000	4.31899700	-3.46987200
H	-0.07652500	5.40939500	-2.09511500
H	1.55194700	4.96875600	-2.61823400
C	2.57712300	3.57953100	-0.01593000
C	3.20339400	3.59174100	1.24587400
C	4.58591500	3.49581000	1.38331300
C	5.40019900	3.36619700	0.25623800
C	4.80379400	3.32879000	-1.00257000
C	3.41685900	3.43140000	-1.13602800
H	2.99602600	3.39027900	-2.13414300
H	5.41654600	3.21754900	-1.89374000
H	6.47868400	3.28454500	0.35991700
H	5.02637000	3.51128300	2.37708600
H	2.59354100	3.67890100	2.13726400
N	-3.26771700	6.96681400	-0.01789500
C	-3.16393500	7.78436800	1.20352200
H	-3.81717400	7.36558000	1.97587400
H	-3.46293200	8.83161600	1.04188300
H	-2.13350200	7.76751700	1.57070400
C	-2.27195900	7.37077600	-1.04415500
H	-2.35288300	6.64778700	-1.86531000
H	-1.28208900	7.23313800	-0.59495700
C	-2.38171600	8.79263400	-1.61159000
H	-1.58635300	8.94479000	-2.34946500
H	-3.33658000	8.96472300	-2.11864800
H	-2.26110000	9.55778100	-0.83793500
C	-4.64598200	7.00177800	-0.53743500
H	-4.99344300	8.02485000	-0.74843600
H	-4.70607400	6.41574100	-1.45935000
H	-5.32052000	6.55444700	0.19739700
H	0.60526400	2.54450700	0.50693600



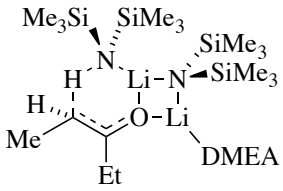


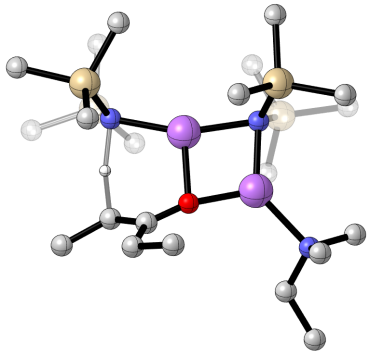
A_2(ketone)(DMEA)
Pro Z
G = –2768.631864
G_{MP2} = –1732561.091

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	1.33079700	-1.34437800	0.22685800
H	1.85812300	-1.56977200	-0.70578000
H	2.07986000	-0.99634300	0.95074600
H	0.92053300	-2.28300700	0.61184900
C	0.93106200	1.49933800	-0.72379900
H	1.45787900	1.26079800	-1.65518600
H	0.26221600	2.34396600	-0.92890200
H	1.68602800	1.84387500	-0.00478900
N	-1.39037200	-0.46430900	-0.97575900
Si	-1.14702300	-0.69730000	-2.69857200
C	-0.98629600	0.93768400	-3.66075100
H	-1.84695300	1.59696800	-3.49973300
H	-0.08878400	1.49894400	-3.38274100

H	-0.92869500	0.73458900	-4.73851800
C	-2.60829700	-1.59907500	-3.51762100
H	-2.40478500	-1.67903500	-4.59340700
H	-2.75573300	-2.61627900	-3.14193100
H	-3.55549600	-1.05999200	-3.41609500
C	0.38490000	-1.73482000	-3.15566900
H	1.32493800	-1.21760200	-2.93185800
H	0.40381900	-2.69623100	-2.62824800
H	0.38081800	-1.94845800	-4.23257500
Li	-2.96802900	0.75066200	-0.44882400
N	-4.22117400	2.42316100	-0.23874600
Si	-3.81735100	3.35979600	1.16612600
C	-2.05467000	4.07926700	1.14489100
H	-1.96616600	4.84699900	0.36641800
H	-1.81207800	4.55559500	2.10400100
H	-1.28330900	3.32803300	0.94643500
C	-3.99947500	2.25040700	2.71151500
H	-3.67237100	2.78466000	3.61263700
H	-5.04947800	1.96824700	2.87953600
H	-3.41508800	1.32480200	2.65623300
C	-4.93307700	4.87101400	1.50999400
H	-4.79475200	5.66404100	0.76534900
H	-6.00017200	4.61908000	1.52727800
H	-4.68051200	5.30175800	2.48812800
Si	-4.59844800	3.16776100	-1.75760000
C	-6.18295600	4.23513000	-1.76445700
H	-7.06355200	3.66176800	-1.44399600
H	-6.10819300	5.10936000	-1.10970100
H	-6.38929100	4.60079200	-2.77925600
C	-4.96014600	1.81284500	-3.05209500
H	-5.15234200	2.25848000	-4.03635300
H	-4.13203400	1.10595100	-3.17533400
H	-5.85649200	1.23636300	-2.78313100
C	-3.21851700	4.27874700	-2.45133500
H	-3.08575400	5.18003100	-1.83960200
H	-2.25286500	3.76027200	-2.47960400
H	-3.44924200	4.60923800	-3.47232400
Li	-5.48472700	0.98718200	0.26391000
O	-4.43411500	-0.58323200	0.02623900
C	-4.27851600	-1.82722000	-0.19156300
C	-5.40481800	-2.51232400	-0.90425100
C	-5.99396300	-3.65851700	-0.34664700
C	-7.11659100	-4.24623200	-0.92842500
C	-7.63310200	-3.68700500	-2.09156200
C	-7.08076400	-2.54756700	-2.67005500
C	-5.98020400	-1.95311600	-2.05737000
H	-5.55197400	-1.05540100	-2.48807300
H	-7.51323200	-2.14351800	-3.57958200
F	-8.70527000	-4.25809900	-2.67101200
H	-7.58809000	-5.12319100	-0.49749700
H	-5.59187900	-4.07503700	0.56976000
C	-3.03077300	-2.48718800	0.17576900
C	-2.63013200	-2.41224800	1.63893500
C	-1.43000100	-3.01307700	2.05902500
C	-1.04251400	-3.01602500	3.39925800
C	-1.84432300	-2.41187500	4.36744400
C	-3.03872200	-1.80892800	3.97113900
C	-3.42524400	-1.81165500	2.63040000
H	-4.35835600	-1.33215300	2.35601300
H	-3.68036600	-1.33379800	4.70915300
H	-1.54408700	-2.40982700	5.41155200
H	-0.10569200	-3.48923200	3.68214800
H	-0.78616200	-3.48971800	1.32800200
C	-2.69426900	-3.83212900	-0.52040400
H	-1.62642800	-3.79712700	-0.77646200
H	-3.20967400	-3.85505200	-1.48590200
C	-2.95577000	-5.16327100	0.20477200
H	-2.54027600	-5.98882500	-0.38538200
H	-2.49077400	-5.19566800	1.19353000
H	-4.02222100	-5.36750300	0.33452500
N	-7.51466400	0.84386900	0.87739400
C	-8.29513000	0.64712600	-0.35730000
H	-8.08770300	1.46924200	-1.04991600
H	-9.38079800	0.62589800	-0.17575800
H	-8.00150100	-0.29252400	-0.83373700
C	-7.60785900	-0.32576700	1.78900100
H	-6.92378400	-0.13116000	2.62463600
H	-7.20670600	-1.18613100	1.24193600
C	-8.99484100	-0.67866000	2.34361900
H	-8.90661100	-1.55651300	2.99312600
H	-9.42118300	0.13148700	2.94395700
H	-9.70641400	-0.92854300	1.54984600
C	-7.92431200	2.09642900	1.53613600
H	-8.99812500	2.11665200	1.77775100
H	-7.35592000	2.23085400	2.46099800
H	-7.70653600	2.93932100	0.87469900
C	-0.52853800	0.52486500	1.74595500
H	-1.30942100	1.29211100	1.74658100
H	-0.88482500	-0.31360600	2.34951800
H	0.33689600	0.96038500	2.26300000
H	-2.22067000	-1.59828600	-0.38462400

Table A.1.10. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for transition states of LiHMDS/DMEA-mediated enolizations of 3-pentanone (3-pent) at –40 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

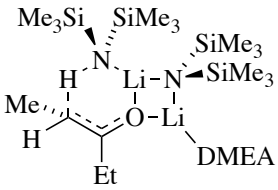


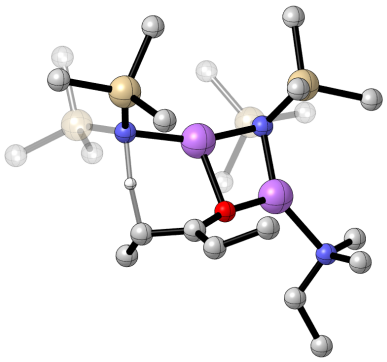


A_2(3-pent)(DMEA)
Pro E
G = –2246.750700
G_{MP2} = –1406041.867

Atom	X	Y	Z	Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000	H	-4.00207200	5.67686000	-2.54731700
N	0.26863300	0.64064800	-1.58791600	C	-3.38245800	2.20768900	-2.54336500
Li	2.00761400	1.74758000	-1.75112100	H	-4.42509500	2.55155000	-2.62687300
Si	0.01858700	-0.30297600	-3.01972400	H	-3.04626600	1.87298600	-3.52816000
C	1.43581000	-1.52004800	-3.38999400	H	-3.35716400	1.35208300	-1.86330700
H	1.46397300	-2.31849400	-2.63842800	O	0.99602200	3.59224000	-1.73557700
H	1.31009000	-1.99622900	-4.37127800	C	1.79483600	4.58777300	-1.76360500
H	2.41908100	-1.03631600	-3.38126900	C	1.64925400	5.69923400	-0.73692500
C	-0.13893700	0.87937600	-4.51390500	C	0.52581400	5.53129600	0.28155500
H	-0.15411300	0.32080800	-5.45841400	H	0.63128200	4.60020100	0.84593800
H	-1.07196500	1.45824900	-4.47424300	H	-0.45291900	5.51819100	-0.20737000
H	0.68781500	1.59685300	-4.57821800	H	0.53217700	6.36351500	0.99335500
C	-1.56161400	-1.37257200	-3.04459200	H	1.52858600	6.64253200	-1.29038300
H	-1.52644600	-2.17424000	-2.29680600	H	2.61207500	5.80227600	-0.22025600
H	-2.46969700	-0.78768800	-2.85602800	C	2.90060500	4.59682100	-2.66891300
H	-1.67651600	-1.85262600	-4.02555300	H	2.62848700	4.14523300	-3.62799100
Li	-0.50065400	2.46546900	-1.76979700	C	3.78978400	5.82520000	-2.80531100
N	-2.48047900	3.25691100	-2.03618700	H	4.24050300	6.11782800	-1.84979800
C	-2.96788400	3.73506900	-0.73131300	H	4.61532300	5.61543000	-3.49312700
H	-2.94865200	2.90880100	-0.01381300	H	3.25633100	6.70255400	-3.19838700
H	-3.99883700	4.11934600	-0.77651600	C	-1.84059100	-0.28092200	0.43149400
H	-2.31700400	4.53038000	-0.35908600	H	-2.42160400	0.65013500	0.37876900
C	-2.30272500	4.36350200	-3.01157200	H	-2.31988000	-1.00479600	-0.23702200
H	-1.85887200	3.92230700	-3.91248500	H	-1.94175100	-0.66272200	1.45609500
H	-1.54987300	5.03956500	-2.58976100	C	0.61017400	1.24958100	1.30389400
C	-3.54981600	5.16736600	-3.40446800	H	0.39200700	0.88770700	2.31683600
H	-3.26515100	5.93650300	-4.13081300	H	1.69070300	1.42593100	1.25196400
H	-4.31548500	4.54072800	-3.87339100	H	0.11410700	2.22408000	1.19595900

C	0.86454100	-1.66042900	0.34671000
H	0.45024600	-2.46680700	-0.27157400
H	1.94106000	-1.61445100	0.14395000
H	0.73694600	-1.95797200	1.39574300
Si	4.86182500	1.59913200	-3.33977400
C	6.28777300	2.73084200	-3.89641700
H	7.08439800	2.79988000	-3.14848700
H	6.73713400	2.35475900	-4.82498600
H	5.93427800	3.75025000	-4.09521500
C	5.57731700	-0.14997100	-3.12629500
H	6.37582400	-0.18616400	-2.37574300
H	4.80672000	-0.86862700	-2.82221900
H	6.00482700	-0.50522400	-4.07307300
N	4.03218600	2.18351000	-1.91015000
Si	4.80982400	2.10837800	-0.34433600
C	4.59019900	0.40621500	0.47279800
H	3.53505000	0.12238000	0.55746700
H	5.09074800	-0.37816300	-0.10692900
H	5.01700800	0.39397600	1.48432800
C	4.05229900	3.41297100	0.81676700
H	4.43040900	3.27484800	1.83759600
H	4.33280200	4.42612400	0.50255700
H	2.95849600	3.36534400	0.86693700
C	6.68006200	2.47169600	-0.33096200
H	7.26348400	1.72827500	-0.88664900
H	6.90830000	3.45696100	-0.75501100
H	7.04865900	2.46494300	0.70344900
C	3.67691600	1.52488200	-4.82542600
H	2.86794400	0.80103700	-4.68446000
H	3.22149100	2.49721100	-5.05038700
H	4.23122900	1.21597500	-5.72132600
H	3.56086600	3.53216400	-2.22340400





A_2(3-pent)(DMEA)
Pro Z
G = = –2246.744211
G_{MP2} = –1406038.748

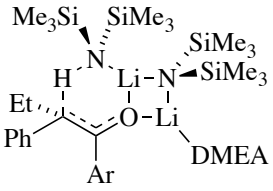
Atom	**X**	**Y**	**Z**
Si	0.00000000	0.00000000	0.00000000
N	-0.25828400	-0.67737400	-1.57682300
Li	-1.93223800	-1.86317000	-1.73567200
Si	-0.03474100	0.27815200	-3.00668400
C	-1.47518100	1.47418700	-3.35659300
H	-1.48153400	2.29162200	-2.62575900
H	-1.39167100	1.92522600	-4.35403000
H	-2.45318200	0.98288500	-3.29568100
C	0.14122800	-0.89041400	-4.50812100
H	0.15866000	-0.32409200	-5.44792500
H	1.07967500	-1.46054900	-4.46450700
H	-0.67944000	-1.61329600	-4.58521500
C	1.53269900	1.36752400	-3.03433900
H	1.50574100	2.15355800	-2.26990000
H	2.44849000	0.78578800	-2.87354100
H	1.62744500	1.86812200	-4.00716700

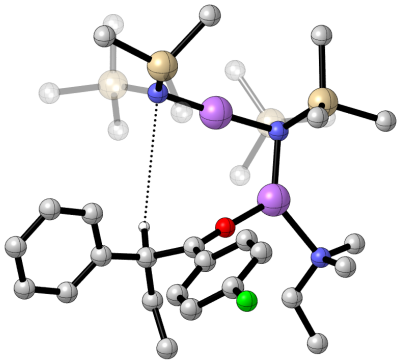
Atom	**X**	**Y**	**Z**
Li	0.59845500	-2.46908100	-1.73747300
N	2.55354500	-3.25747800	-2.09980200
C	3.00283700	-3.88686000	-0.84705300
H	2.96916800	-3.15002200	-0.03777600
H	4.03194200	-4.27367700	-0.90849200
H	2.33581400	-4.71495900	-0.59126800
C	2.37803000	-4.25067500	-3.19116000
H	1.96727000	-3.70769100	-4.05070000
H	1.60109300	-4.94942500	-2.85976200
C	3.62005300	-5.03585500	-3.63452400
H	3.34068100	-5.72083500	-4.44251200
H	4.40894000	-4.38056000	-4.01784700
H	4.04013000	-5.63909600	-2.82310200
C	3.47855400	-2.17345400	-2.47430600
H	4.51702800	-2.52221300	-2.58528100
H	3.15811800	-1.72484700	-3.41838400

H	3.45774600	-1.39936500	-1.70241000
O	-0.81498500	-3.67338300	-1.58849300
C	-1.59896300	-4.67478000	-1.48050400
C	-1.41281300	-5.65976500	-0.33477700
C	-0.55617400	-5.20847600	0.84643300
H	-1.01031000	-4.36696600	1.37618000
H	0.44146600	-4.89782200	0.52330200
H	-0.43804600	-6.02975400	1.56163800
H	-0.96827000	-6.55941400	-0.79093100
H	-2.40401400	-5.98003600	0.00616600
C	-2.68367200	-4.86403900	-2.38905900
H	-3.28105000	-5.75084300	-2.16007500
C	-2.38652000	-4.73012300	-3.88317200
H	-1.87484100	-5.62367500	-4.26735100
H	-3.30648700	-4.60789100	-4.46212600
H	-1.74496600	-3.86857900	-4.08823000
C	1.84907300	0.18648300	0.44869100
H	2.36286400	-0.78546900	0.45376500
H	2.38336800	0.83771500	-0.25247100
H	1.96773000	0.61451100	1.45284700
C	-0.70027800	-1.15368400	1.34259700
H	-0.47089900	-0.75877300	2.34074400
H	-1.78935400	-1.26192900	1.28327200
H	-0.26453400	-2.15894400	1.28318900
C	-0.78795200	1.71049600	0.27795900
H	-0.34477100	2.47904800	-0.36705900
H	-1.86646700	1.69759000	0.07845000
H	-0.64776700	2.03729800	1.31659100
Si	-4.78826400	-1.87093600	-3.41114200
C	-6.05253000	-3.15894200	-4.01889900
H	-6.85150500	-3.32863000	-3.28883500
H	-6.52368700	-2.82645300	-4.95321400
H	-5.58144900	-4.12961800	-4.21757100
C	-5.73205000	-0.23803400	-3.14305800
H	-6.51445400	-0.30790100	-2.37953200
H	-5.05608100	0.57495200	-2.85054400
H	-6.21843200	0.06273500	-4.08029700
N	-3.92488200	-2.41167300	-1.97337700
Si	-4.76804200	-2.29906300	-0.43435900
C	-4.67559100	-0.54698800	0.29941700
H	-3.64369800	-0.17998700	0.35538600
H	-5.24406200	0.17414300	-0.29792300
H	-5.08577500	-0.52958300	1.31780900
C	-3.98925800	-3.47802100	0.83608800
H	-4.45922000	-3.32163000	1.81531400
H	-4.15137900	-4.52687700	0.56162100
H	-2.91366500	-3.32302700	0.96671300
C	-6.60804800	-2.79299000	-0.46569400
H	-7.22194400	-2.14737300	-1.10293900
H	-6.74182000	-3.82498400	-0.81235700
H	-7.01874600	-2.73218100	0.55089600
C	-3.64525100	-1.51797400	-4.88730700
H	-2.90754000	-0.73888900	-4.67094300
H	-3.10843300	-2.40066400	-5.24649900
H	-4.25903900	-1.15254200	-5.72141900
H	-3.40702800	-3.73458300	-2.13001600

VI. Intrinsic reaction coordinate (IRC) computations

Table A.1.11. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for the forward and reverse IRC calculations of LiHMDS/DMEA-mediated enolization transition structures at –40 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.) The 2D representations below correspond to the transition state, which the IRC has been done.



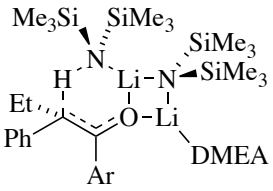


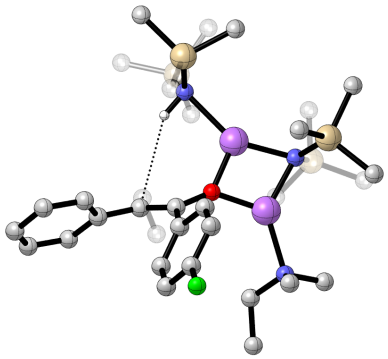
Reverse IRC of A_2(3-pent)(DMEA) Pro E
G = –2768.667589
G_{MP2} = –1732576.735

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	1.71018800	-0.75417800	-0.39200700
H	1.98263900	-1.56038800	0.29738700
H	1.70534600	-1.17904500	-1.40517500
H	2.50648400	-0.00136400	-0.35678100
C	-1.22642400	-1.45978100	-0.13309900
H	-1.03690800	-2.19314700	0.66201200
H	-2.26800900	-1.13180200	-0.02392800
H	-1.14255700	-1.98765600	-1.09268900
N	-0.14417000	0.89087000	1.45848000
Si	0.33060000	0.35400900	3.01690600
C	-1.15850700	-0.11416400	4.11923600
H	-1.84304000	0.72814600	4.27880900
H	-1.74018600	-0.92021400	3.65305700
H	-0.83902600	-0.46476200	5.10993200
C	1.28326200	1.71339600	3.96710900
H	1.48410800	1.41383100	5.00438100
H	2.25093100	1.92290100	3.49301200
H	0.73128500	2.66146500	4.00269400
C	1.47565000	-1.17389800	3.08434800
H	1.02359500	-2.05267400	2.60791400
H	2.44007100	-0.99423900	2.59451100
H	1.68118900	-1.43955300	4.13002100

Atom	X	Y	Z
C	-0.33458700	1.14423500	-1.49820900
H	-1.28716100	1.68354300	-1.43589400
H	0.46571000	1.89058700	-1.59490600
H	-0.35487500	0.57017400	-2.43382100
Li	-1.50358600	2.23644900	1.39932900
N	-3.00785900	3.63554500	1.38810400
Si	-3.97387600	3.34761100	-0.03037900
C	-4.19797000	1.50175800	-0.42557000
H	-4.77290900	1.00541500	0.36612000
H	-4.74564200	1.36324600	-1.36701200
H	-3.24859400	0.96349900	-0.52115900
C	-3.10597200	4.16159600	-1.52839700
H	-3.61737500	3.89758600	-2.46270500
H	-3.11792400	5.25926900	-1.46539700
H	-2.06162900	3.84189500	-1.63581200
C	-5.73842000	4.06929500	-0.00364700
H	-6.36087600	3.60567600	0.77121000
H	-5.75238300	5.15219000	0.16698100
H	-6.22965300	3.88073900	-0.96727900
Si	-3.69134200	3.62029100	2.98746400
C	-4.92368500	5.02763300	3.37018000
H	-4.44825700	6.01614500	3.32491200
H	-5.78120900	5.03928000	2.68897300

H	-5.31587200	4.91044200	4.38910000
C	-2.29761600	3.86066100	4.26426700
H	-2.69260900	3.79699300	5.28619700
H	-1.49958500	3.11411500	4.18219200
H	-1.83617800	4.85347500	4.16276000
C	-4.60736300	2.00676000	3.40580300
H	-5.50634700	1.88594700	2.78799000
H	-3.98005800	1.12186100	3.24618300
H	-4.93056900	1.99609400	4.45474400
Li	-1.88328700	5.20602200	0.95496400
O	0.01783400	5.09632000	0.91944700
C	1.25833000	5.06959200	0.89780700
C	2.00644300	5.51220500	2.10046700
C	3.37073500	5.85970800	2.08016000
C	4.00351300	6.32897700	3.22618100
C	3.27078300	6.42475200	4.40507400
C	1.92472900	6.07193200	4.47204000
C	1.30068900	5.62408900	3.31611500
H	0.25793500	5.33201300	3.34818800
H	1.39605600	6.14126000	5.41659000
F	3.88172300	6.86576900	5.51508600
H	5.05160500	6.60795600	3.22189600
H	3.94659400	5.76487600	1.16978300
C	1.91276400	4.60880800	-0.41645600
C	1.84968600	5.76425500	-1.46059900
H	0.78868000	5.95802600	-1.65357700
H	2.26007500	5.37506300	-2.39937100
C	2.53134100	7.09197900	-1.10357300
H	2.40072500	7.80784200	-1.92290300
H	2.10128900	7.54371900	-0.20205800
H	3.60675800	6.98467000	-0.93258500
C	3.24129000	3.86786000	-0.28645500
C	3.29007400	2.74112100	0.55085100
C	4.46697300	2.00738500	0.69251800
C	5.61663400	2.37667900	-0.00975400
C	5.57219900	3.47594900	-0.86560400
C	4.39290800	4.21350000	-1.00536000
H	4.38392100	5.05639800	-1.68860600
H	6.45338200	3.76265800	-1.43368600
H	6.53314600	1.80331600	0.09898900
H	4.47868700	1.13787600	1.34367400
H	2.39162800	2.41617600	1.07281000
N	-2.30784300	7.33178800	0.78842400
C	-1.90546000	7.86137000	2.10270900
H	-2.45870200	7.33708100	2.88855300
H	-2.10629800	8.93833700	2.21226700
H	-0.83581900	7.68818300	2.25555500
C	-1.47352400	7.88167400	-0.30909800
H	-1.76601100	7.35342900	-1.22498400
H	-0.43967800	7.59364800	-0.09267400
C	-1.53784600	9.39526800	-0.55766100
H	-0.86707200	9.64978700	-1.38573500
H	-2.54254800	9.72844500	-0.83659000
H	-1.21530900	9.97369000	0.31442400
C	-3.74266500	7.57471600	0.55946000
H	-4.00710000	8.64188800	0.61821100
H	-4.02467200	7.20010700	-0.42868000
H	-4.32657700	7.03609200	1.30914800
H	1.18895900	3.86775800	-0.77898400





Forward IRC of A_2(3-pent)(DMEA) Pro E

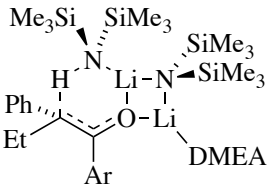
G = = –2768.704483

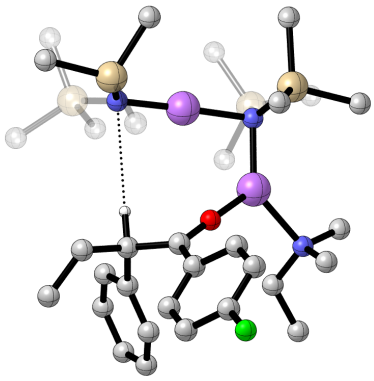
G_{MP2} = –1732603.562

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	0.82829000	-1.66255100	-0.36791800
H	0.83405800	-2.33601400	0.49493300
H	0.30235900	-2.17322500	-1.18478300

H	1.86802900	-1.52351200	-0.69011000
C	-1.75511800	-0.27295500	0.64238800
H	-1.79219300	-0.92013100	1.52526200
H	-2.25211800	0.67076400	0.89319800
H	-2.35178500	-0.75853700	-0.13985200
N	0.93336800	0.92227800	1.23224600
Si	0.90582300	0.45547100	2.96936100
C	-0.64086700	1.15950100	3.78796100
H	-0.73612300	2.23973500	3.63996100
H	-1.55425500	0.69182000	3.40559200
H	-0.60732000	0.97586300	4.86933200
C	2.47380900	1.15726800	3.74893400
H	2.51386300	0.90025100	4.81468100
H	3.37309600	0.74218400	3.27749200
H	2.53428100	2.24678100	3.67160000
C	0.92964100	-1.41831300	3.25730700
H	0.04487600	-1.92928900	2.86136300
H	1.81567000	-1.88865300	2.81524100
H	0.95979800	-1.61426800	4.33711700
C	-0.08651100	0.93510200	-1.63754500
H	-0.46760800	1.95463700	-1.53499700
H	0.88718000	0.98524400	-2.13581300
H	-0.76790500	0.40050500	-2.31249500
Li	1.00802700	3.19814800	1.02637100
N	-0.02114400	4.98313900	1.01268300
Si	-1.04943400	5.13633000	-0.37291800
C	-2.46733400	3.86055800	-0.42157000
H	-3.19155600	4.05898400	0.37753600
H	-3.01029100	3.90081400	-1.37502100
H	-2.11435900	2.83184000	-0.28605200
C	-0.00653100	4.90129800	-1.95589300
H	-0.64737500	4.84391100	-2.84510600
H	0.67632800	5.74782800	-2.11263800
H	0.60744000	3.99278300	-1.93799800
C	-1.91774100	6.82281300	-0.58462600
H	-2.64315700	7.01801300	0.21473100
H	-1.20927900	7.65968000	-0.59640000
H	-2.46993800	6.84538600	-1.53359000
Si	-0.52397700	5.57088200	2.56200100
C	-0.53169300	7.47414400	2.71938000
H	0.46651200	7.89699600	2.54278200
H	-1.22002500	7.95006100	2.01230600
H	-0.83485800	7.77858900	3.72997400
C	0.68763800	5.00458300	3.92196500
H	0.30505900	5.28364700	4.91214900
H	0.85287800	3.92068100	3.93601500
H	1.66658900	5.48702200	3.80913200
C	-2.26461900	5.00751700	3.10150800
H	-3.04593600	5.43892000	2.46336700
H	-2.38019500	3.91739600	3.06407100
H	-2.47517300	5.32757100	4.13043100
Li	1.88969300	5.48302800	0.54584400
O	2.73531500	3.82597100	0.65710500
C	3.99655000	3.38555600	0.68221800
C	4.88820200	4.12483400	1.64019300
C	6.17460300	4.55469200	1.26641700
C	6.96989200	5.30832300	2.12850200
C	6.47175900	5.63667800	3.38477100
C	5.20234200	5.24355300	3.79140800
C	4.41749100	4.50108400	2.90854200
H	3.41892500	4.20719600	3.20881500
H	4.84358000	5.51930300	4.77810400
F	7.23775700	6.36430800	4.22719800
H	7.96132700	5.64268600	1.83997400
H	6.55811700	4.29145800	0.28651000
C	4.45937700	2.39812400	-0.15578300
C	3.58500300	1.95740400	-1.32011500
H	2.54129800	1.91196400	-0.99393800
H	3.86337800	0.94177900	-1.62853500
C	3.64148800	2.89210800	-2.54421400
H	2.98630900	2.53282800	-3.34828400
H	3.31545200	3.89979600	-2.26828800
H	4.65642500	2.96925600	-2.94986500
C	5.76066200	1.70451500	0.01061100
C	6.24129100	1.31565400	1.27947200
C	7.43824600	0.61894400	1.42602200
C	8.19444500	0.26469000	0.30599200
C	7.72904500	0.61690400	-0.96137300
C	6.53350900	1.32079900	-1.10543900
H	6.19919600	1.58687500	-2.10390900
H	8.29999300	0.34581300	-1.84645100
H	9.12470700	-0.28551900	0.41956300
H	7.77414600	0.33660800	2.42109500
H	5.65694200	1.56106700	2.16097600
N	2.86843100	7.29405600	-0.04482900
C	3.57877700	7.80080200	1.14253100
H	2.85967700	7.95775500	1.95339400
H	4.08776500	8.75939300	0.95483000
H	4.31848600	7.06776800	1.47277700
C	3.80474000	6.87042600	-1.11787900
H	3.19253700	6.43557000	-1.91758300
H	4.41245600	6.05814400	-0.70623900

C	4.72525500	7.94404500	-1.71505000
H	5.34316100	7.48879800	-2.49693500
H	4.16478200	8.76418200	-2.17563700
H	5.40318300	8.36902300	-0.96770400
C	1.89950500	8.29546200	-0.51771800
H	2.37050100	9.26101200	-0.76075000
H	1.38960500	7.92338000	-1.41116800
H	1.14937200	8.46822100	0.25891700
H	1.91472800	0.96333500	0.93632100



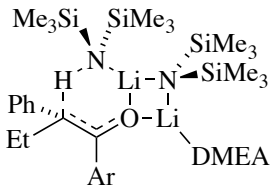


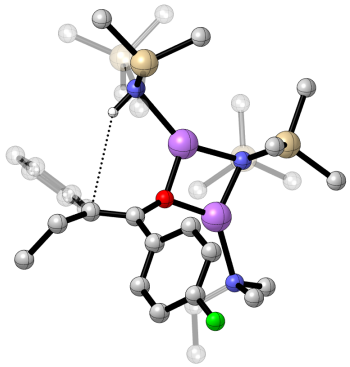
Reverse IRC of A$_2$(3-pent)(DMEA) Pro Z
G = –2768.663811
G_{MP2} = –1732573.969

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	-1.14098700	-1.43377500	0.55068800
H	-1.19188900	-2.23242300	-0.19807400
H	-0.78605300	-1.88459700	1.48736600
H	-2.16762700	-1.08499200	0.72730500
C	1.77516500	-0.70422700	0.00997300
H	1.90517100	-1.50080600	-0.73309500
H	2.50657900	0.08024700	-0.22484000
H	2.04134500	-1.12304500	0.98983200
N	-0.45849300	0.76737300	-1.46095200
Si	-0.50281000	0.01405800	-3.00264700
C	0.89822600	0.64113600	-4.14041200
H	0.87921000	1.73152900	-4.26758600
H	1.87589900	0.38499200	-3.71179200
H	0.84725100	0.19654000	-5.14342700
C	-2.14441600	0.37350000	-3.91647400
H	-2.11536200	0.01788000	-4.95500600
H	-2.97828100	-0.13817300	-3.41892100
H	-2.38540400	1.44352700	-3.94486100
C	-0.35482800	-1.89041400	-3.03890300
H	0.56886700	-2.25022900	-2.57035200
H	-1.19466000	-2.38222900	-2.53326700
H	-0.34989700	-2.24285700	-4.07908400
Li	-0.39447200	2.66848800	-1.55542600

Atom	X	Y	Z
N	-0.39281200	4.70290300	-1.66493200
Si	0.58408200	5.22301600	-0.32064900
C	2.15930300	4.17350500	-0.10731400
H	2.86014700	4.36044300	-0.93005900
H	2.67609900	4.42102700	0.82917100
H	1.96044100	3.09511800	-0.09418000
C	-0.43999600	5.07716700	1.28262000
H	0.18451500	5.26799900	2.16453300
H	-1.25701800	5.81078100	1.30881100
H	-0.88032400	4.08139300	1.41315300
C	1.19636900	7.02775800	-0.38403800
H	1.88838400	7.20110000	-1.21702400
H	0.37553200	7.74806300	-0.48145700
H	1.73798600	7.26847600	0.54026600
Si	-0.01025000	5.19507700	-3.28954300
C	-0.34331300	7.03910300	-3.66175700
H	-1.40580700	7.29142800	-3.54100800
H	0.23212200	7.71488200	-3.01993100
H	-0.07782500	7.26856500	-4.70226200
C	-1.12200700	4.26494900	-4.52310500
H	-0.87624400	4.55129000	-5.55367500
H	-1.02325300	3.17623300	-4.45755700
H	-2.18103300	4.51061300	-4.36527100
C	1.79583200	4.86817600	-3.79071500

H	2.49795800	5.47876400	-3.20948500
H	2.07534800	3.81789100	-3.64270500
H	1.95791300	5.10568200	-4.85007000
Li	-2.32490400	4.90545900	-1.26129600
O	-3.57859900	3.48493800	-1.60301200
C	-4.41207000	2.56869500	-1.62422200
C	-5.43938200	2.57246700	-2.70182100
C	-6.67491700	1.90926200	-2.59172300
C	-7.62455200	1.99103800	-3.60551200
C	-7.31882700	2.72179900	-4.74924000
C	-6.10038000	3.37888000	-4.90425500
C	-5.17237200	3.30740600	-3.87367800
H	-4.21430500	3.80332500	-3.97475400
H	-5.89695200	3.92488900	-5.81922800
F	-8.22543300	2.79275200	-5.73590000
H	-8.58565500	1.49464200	-3.52612900
H	-6.91199800	1.33641300	-1.70448600
C	-4.30197600	1.49063500	-0.53465600
C	-4.87649600	2.00845700	0.78829400
C	-4.15974900	1.78030300	1.97237500
C	-4.65550300	2.20277700	3.20649400
C	-5.87944000	2.86998200	3.28122400
C	-6.60109700	3.10883600	2.11144100
C	-6.10459500	2.68113700	0.87761300
H	-6.68560700	2.88151600	-0.01824500
H	-7.55622900	3.62596300	2.15490000
H	-6.26638200	3.20041400	4.24120800
H	-4.08082100	2.01145900	4.10861200
H	-3.20594100	1.26223400	1.92616900
C	-4.74062600	0.03264300	-0.92504800
H	-3.85335500	-0.59695600	-0.80833600
H	-4.97642800	-0.00302200	-1.99309600
C	-5.87925000	-0.60633800	-0.12077100
H	-6.06368200	-1.62061300	-0.49162400
H	-5.62671700	-0.67922200	0.94151800
H	-6.82388500	-0.05365600	-0.18603400
N	-3.57548900	6.59415600	-0.77904800
C	-4.42627700	6.76814400	-1.96840100
H	-3.79101300	6.93467100	-2.84501600
H	-5.11164900	7.62588000	-1.88348200
H	-5.01466400	5.86177900	-2.13439300
C	-4.36362900	6.20015000	0.41793100
H	-3.64350500	6.00281300	1.22080700
H	-4.84327600	5.24387200	0.18567600
C	-5.42283700	7.18905400	0.92337800
H	-5.92158400	6.75501000	1.79673900
H	-4.98723500	8.14437600	1.23365100
H	-6.19307400	7.39215700	0.17191600
C	-2.78747900	7.81601000	-0.54312800
H	-3.41931600	8.70890700	-0.41692200
H	-2.17619500	7.69260300	0.35488400
H	-2.11948700	7.98580800	-1.39144100
C	-0.05769600	1.22457700	1.46679500
H	0.70279100	2.01070500	1.39535400
H	-1.03393200	1.72063600	1.55000200
H	0.11838500	0.69582900	2.41298600
H	-3.21511900	1.44531500	-0.39907500





Forward IRC of A_2(3-pent)(DMEA) Pro Z
G = –2768.703958
G_{MP2} = –1732606.113

Atom	X	Y	Z
Si	0.00000000	0.00000000	0.00000000
C	1.17857600	-1.47805100	0.13213400
H	1.58302300	-1.80100900	-0.83195900
H	2.02768300	-1.21428500	0.77616800

H	0.67609500	-2.33646800	0.59406300
C	0.88334000	1.44032500	-0.84479100
H	1.34493700	1.15230000	-1.79597500
H	0.20751700	2.28072400	-1.03839500
H	1.68698700	1.80740900	-0.19438600
N	-1.48263900	-0.39252600	-0.94125400
Si	-1.42685400	-0.71329500	-2.70775800
C	-1.26743100	0.91562600	-3.64911500
H	-2.01223000	1.65386500	-3.33584800
H	-0.27888300	1.36939700	-3.52317700
H	-1.41053300	0.73769200	-4.72262000
C	-3.02345000	-1.60118400	-3.17446900
H	-3.00263600	-1.87739200	-4.23604100
H	-3.16127900	-2.52126200	-2.59481500
H	-3.90990600	-0.98175700	-3.01240700
C	0.01403100	-1.83043600	-3.22748400
H	0.99217700	-1.36073500	-3.07531100
H	0.01254900	-2.78385000	-2.68640500
H	-0.07211000	-2.05941600	-4.29768800
Li	-3.34273600	0.80087000	-0.35242300
N	-4.12509600	2.71172600	-0.06386200
Si	-3.53200400	3.51653500	1.35267900
C	-1.69638600	4.03434400	1.26490100
H	-1.57547300	4.89666900	0.59783400
H	-1.32370800	4.33447400	2.25329800
H	-1.03682000	3.24591700	0.88936200
C	-3.75969300	2.36067200	2.85639100
H	-3.27952100	2.77804800	3.75062100
H	-4.82461700	2.23489400	3.09854900
H	-3.34453600	1.35816600	2.70020900
C	-4.41484200	5.14216700	1.82592600
H	-4.21501100	5.93635400	1.09668200
H	-5.50223800	5.03504500	1.90497800
H	-4.04605400	5.49734500	2.79760700
Si	-4.41345400	3.59053400	-1.52780400
C	-5.85719500	4.83882000	-1.44325000
H	-6.79358800	4.34805500	-1.14476400
H	-5.67460400	5.65409400	-0.73467000
H	-6.03104500	5.29172700	-2.42853700
C	-4.93563200	2.41123600	-2.93433200
H	-4.95431300	2.94961900	-3.89065200
H	-4.26864700	1.55039400	-3.06377700
H	-5.94748500	2.02258000	-2.76591200
C	-2.91301800	4.58021800	-2.16496700
H	-2.67204500	5.41935800	-1.50093000
H	-2.01153300	3.95975200	-2.24238400
H	-3.11387200	5.00034400	-3.15914800
Li	-5.63195600	1.43792200	0.42232300
O	-4.87326300	-0.22621900	0.04489000
C	-5.32518700	-1.46716000	-0.15064500
C	-6.58099600	-1.53800100	-0.97909800
C	-7.70262800	-2.27459400	-0.55897100
C	-8.88746200	-2.29036500	-1.29718700
C	-8.94985800	-1.55537500	-2.47487600
C	-7.86980100	-0.80259700	-2.92252700
C	-6.70037400	-0.79245000	-2.16319200
H	-5.86240700	-0.19266600	-2.49521700
H	-7.95290500	-0.23927700	-3.84667000
F	-10.0908770	-1.56572800	-3.19780700
H	-9.75399800	-2.85644800	-0.97037600
H	-7.64921400	-2.83909600	0.36638300
C	-4.72989400	-2.60435100	0.34253800
C	-3.67223100	-2.54855200	1.38541600
C	-2.56538100	-3.42363000	1.37479000
C	-1.66031700	-3.47599400	2.43817200
C	-1.83265400	-2.65586000	3.55333000
C	-2.91468900	-1.76971900	3.58043700
C	-3.81052600	-1.71385800	2.51559000
H	-4.65672600	-1.03684900	2.56142700
H	-3.06774400	-1.12532100	4.44285100
H	-1.13950500	-2.70643200	4.38864000
H	-0.82687600	-4.17356200	2.39772600
H	-2.42035200	-4.09513000	0.53277700
C	-5.09435200	-4.00156100	-0.14671000
H	-4.19985200	-4.47528700	-0.58030200
H	-5.80390500	-3.93425800	-0.97486900
C	-5.65135800	-4.95218900	0.92804600
H	-5.85664200	-5.94263500	0.50378800
H	-4.94379700	-5.08061900	1.75390700
H	-6.58627600	-4.56993200	1.35517400
N	-7.58733300	1.70412900	1.27106200
C	-8.54499800	1.60259500	0.15555100
H	-8.29969400	2.35744100	-0.59897200
H	-9.58538900	1.77214000	0.47485600
H	-8.47498700	0.61515800	-0.30584300
C	-7.73449300	0.58726600	2.23923500
H	-6.93628000	0.70579200	2.98278700
H	-7.52323000	-0.33627200	1.69056400
C	-9.08246700	0.45460000	2.96167200
H	-9.04027700	-0.40278400	3.64260800
H	-9.32238200	1.33845400	3.56185800
H	-9.90798200	0.27956800	2.26407400

C	-7.71425200	3.01892600	1.91904800
H	-8.73175700	3.21107300	2.29459400
H	-7.01483200	3.08879300	2.75697200
H	-7.46384000	3.80144500	1.19776000
C	-0.48191200	0.45350200	1.76076300
H	-1.17268100	1.29770700	1.81587400
H	-0.94323900	-0.39613100	2.27400100
H	0.41669400	0.73151100	2.32697000
H	-1.95248300	-1.18166800	-0.48185400

Chapter 1 References and Footnotes

1. Lai, A.; Kahraman, M.; Govek, S.; Nagasawa. J.; Bonnefous, C.; Julien, J.; Douglas, K.; Sensintaffar, J.; Lu, N.; Lee, K.-j; Aparicio, A.; Kaufman, J.; Qian, J.; Shao, G.; Prudente, R.; Moon, M. J.; Joseph, J. D.; Darimont, B.; Brigham, D.; Grillot, K.; Heyman, R.; Rix, P. J.; Hager, J. H.; Smith, N. D. *J. Med. Chem.* **2015**, *58*, 4888.

2. (a) DeGregorio, M. W.; Wiebe, V. J. Tamoxifen and Breast Cancer, 2nd ed.; Yale University Press: New Haven, CT, 1999. (b) Levenson, A. S.; Jordan, V. C. *Eur. J. Cancer* **1999**, *35*, 1628.

3. McCague, R.; Leclercq, G.; Legros, N.; Goodman, J.; Blackburn, G. M.; Jarman, M.; Foster, A. B. *J. Med. Chem.* **1989**, *32*, 2527.

4. Connor, C. E.; Norris, J. D.; Broadwater, G.; Willson, T. M.; Gottardis, M. M.; Dewhirst, M. W.; McDonnell, D. P. *Cancer Res.* **2001**, *61*, 2917.

5. Li, B. X.; Le, D. N.; Mack, K. A.; McClory, A.; Lim, N.-K.; Cravillion, T.; Savage, S.; Han, C.; Collum, D. B.; Zhang, H.; Gosselin, F. *J. Am. Chem. Soc.* **2017**, *139*, 10777.

6. Early examples of E/Z enolization selectivityies: (a) Masamune, S.; Ellingboe, J. W.; Choy, W. *J. Am. Chem. Soc.* **1982**, *104*, 5526. (b) Gaudemar, M.; Bellassoued, M. *Tetrahedron Lett.* **1989**, *30*, 2779. (c) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066. (d) McCarthy, P. A.; Kageyama, M. *J. Org. Chem.* **1987**, *52*, 4681. (e) Davis, F. A.; Sheppard, A. C.; Chen, B.-C.; Haque, M. S. *J. Am. Chem. Soc.* **1990**, *112*, 6679.

7. Zhao, P.; Condo, A.; Keresztes, I.; Collum, D. B. *J. Am. Chem. Soc*. **2004**, *126*, 3113.

8. (a) Godenschwager, P.; Collum, D. B. *J. Am. Chem. Soc.* **2008**, *130*, 8726. (b) Zhao, P.; Collum, D. B. *J. Am. Chem. Soc.* **2003**, *125*, 14411. (c) Snaddon, T. N.; Buchgraber, P.; Schulthoff, S.; Wirtz, C.; Mynott, R.; Furstner, A. *Chem. Eur. J.* **2010**, *16*, 12133.

9. (a) Tomasevich, L. L.; Collum, D. B. *J. Am. Chem. Soc.* **2014**, *136*, 9710. (b) Romesberg, F. E.; Bernstein, M. P.; Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. *J. Am. Chem. Soc.* **1993**, *115*, 3475.

10. Lucht, B. L.; Collum, D. B. *J. Am. Chem. Soc.* **1995**, *117*, 9863.

11. Lucht, B. L.; Collum, D. B. *J. Am. Chem. Soc.* **1996**, *118*, 2217.

12. (a) Collum, D. B.; McNeil, A. J.; Ramírez, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3002. (b) Algera, R. F.; Gupta, L.; Hoepker, A. C.; Liang, J.; Ma, Y.; Singh, K. J.; Collum, D. B. *J. Org. Chem.* **2017**, *82*, 4513.

13. Frisch, M. J. et al. *GaussianVersion 3.09*; revision A.1; Gaussian, Inc.: Wallingford, CT, 2009.

14. (a) Renny, J. S.; Tomasevich, L. L.; Tallmadge, E. H.; Collum, D. B. *Angew. Chem., Int. Ed.* **2013**, *52*, 11998. (b) Liou, L. R.; McNeil, A. J.; Ramírez, A.; Toombes, G. E. S.; Gruver, J. M.; Collum, D. B. *J. Am. Chem. Soc.* **2008**, *130*, 4859.

15. Measuring the mole fraction within only the ensemble of interest rather than the overall mole fraction of lithium alkoxides added to the samples eliminates the distorting effects of impurities.

16. Job, P. *Ann. Chim.* **1928**, *9*, 113.

17. “CYLview, 1.0b; Legault, C. Y., Université de Sherbrooke, 2009 (http://www.cylview.org).”

18. Rein, A. J.; Donahue, S. M.; Pavlosky, M. A. *Curr. Opin. Drug Discovery Dev.* **2000**, *3*, 734.

19. Casado, J.; Lopez-Quintela, M. A.; Lorenzo-Barral, F. M. *J. Chem. Educ.* **1986**, *63*, 450.

20. Reyes-Rodríguez, G. J.; Algera, R. F.; Collum, D. B. *J. Am. Chem. Soc.* **2017**, *116*, 1233.

21. The rate law provides the stoichiometry of the transition structure relative to that of the reactants: Edwards, J. O.; Greene, E. F.; Ross, J. *J. Chem. Educ.* **1968**, *45*, 381.

22. (a) Gregory, K.; Schleyer, P. v. R.; Snaith, R. *Adv. Inorg. Chem.* **1991**, *37*, 47. (b) Mulvey, R. E. *Chem. Soc. Rev.* **1991**, *20*, 167.

23. (a) Lucht, B. L.; Bernstein, M. P.; Remenar, J. F.; Collum, D. B. *J. Am. Chem. Soc.* **1996**, *118*, 10707. (b) Liang, J.; Hoepker, A. C.; Algera, R. F.; Ma, Y.; Collum, D. B. *J. Am. Chem. Soc.* **2015**, *137*, 6292. (c) Plessel, K. N.; Jones, A. C.; Wherritt, D. J.; Maksymowicz, R. M.; Poweleit, E. T.; Reich, H. J. *Org. Lett.* **2015**, *17*, 2310.

24. Tomioka, H.; Hayashi, N.; Izawa, Y.; Senthilnathan, V. P.; Platz, M. S. *J. Am. Chem. Soc.* **1983**, *105*, 5053.

CHAPTER 2

A CASE FOR LITHIUM TETRAMETHYLPIPERIDIDE-MEDIATED ORTHOLITHIATIONS: REACTIVITY AND MECHANISMS

A Case for Lithium Tetramethylpiperidide-Mediated Ortholithiations:

Reactivity and Mechanisms

Abstract

Rate and mechanistic studies of ortholithiations by lithium 2,2,6,6-tetramethylpiperidine focus on four arenes: 1,4-bis(trifluoromethyl)benzene, 1,3-bis(trifluoromethyl)benzene, 1,3-dimethoxybenzene, and 4,4-dimethyl-2-phenyl-2-oxazoline. Metalations occur via substrate-dependent combinations of monosolvated monomer, disolvated monomer, and tetrasolvated dimer (triple ions). Density functional theory computational studies augment the experimental data. We discuss the challenges presented by shifting dimer–monomer proportions in determining the observable reaction orders and our mathematical treatment of such shifting in reactant structure.

Introduction

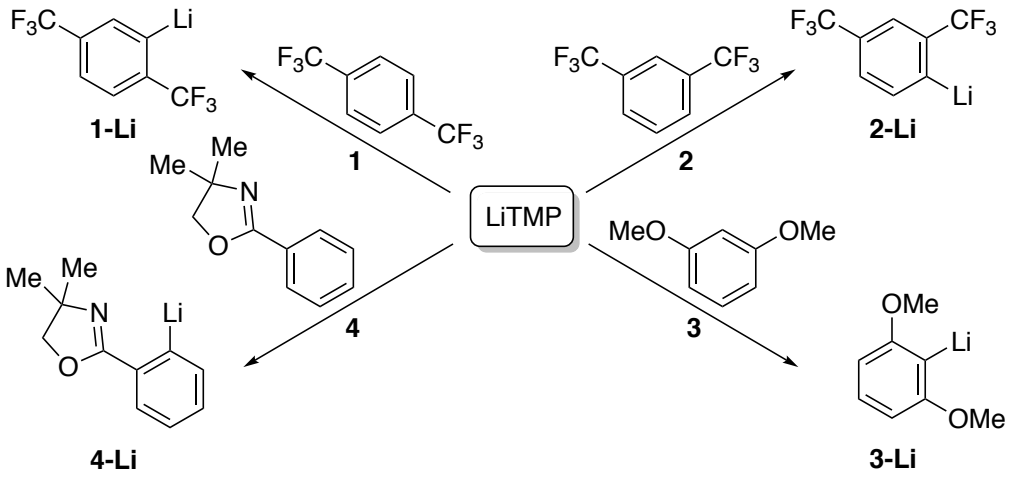
Few transformations are more important than functionalizations of C–H bonds on aromatic and heteroaromatic rings. [1] Traditional electrophilic aromatic substitutions are limited to electron-rich aromatics, have marginal regioselectivities, and can generate noxious waste streams when used on scale.[2] Emergent efforts to achieve catalytic transition-metal-mediated C–H activations are making great strides but remain in the early to mid-developmental stages.[3] Ortholithiations with subsequent trapping by electrophiles are not without limitations but generally offer high reactivities of organolithium bases and exceptional regiocontrol.[4,5]

The choice of base for orthometalations has chemical, economic, and safety consequences. Lithium diisopropylamide (LDA) is ideal for relatively acidic, multi-functional arenes.[5] Less reactive arenes are most often metalated using *n*- or *sec*-butyllithium facilitated by a variety of accelerants such as tetrahydrofuran (THF) or *N,N,N',N'*-tetramethylethylenediamine. There are, however, some large disparities separating LDA and alkyllithiums: the high basicity and reactivity offered by alkyllithiums is offset by functional group incompatibilities. Note that

casual mentions of basicity and reactivity can connote kinetic or thermodynamic effects depending on context. Does a base observably metalate (thermodynamic) and, if so, how fast (kinetic)?

Nestled between LDA and alkyllithiums lies lithium 2,2,6,6-tetramethylpiperidide (LiTMP).[6] This base *has* been used for many ortholithiations, of course, but we sense that many practitioners are unaware of its advantages. *LiTMP is not simply a more expensive equivalent of LDA*. LiTMP-mediated metalations have a greater driving force[7,8] *and* disproportionately higher metalation rates, both of which may stem from high steric demands that inhibit stabilizing aggregation—a form of ground-state destabilization. The high steric demands also amplify sterically dictated regiocontrol, and the hindered 2,2,6,6-tetramethylpiperidine (TMPH) byproduct precludes regiochemical equilibrations that are readily mediated by *i*-Pr_2NH.[9,10,11] The higher cost of TMPH is also a red herring. TMPH is significantly more expensive than *i*-Pr_2NH, but current prices are markedly lower in bulk and should be susceptible to further downward pressure given that the compound is prepared from acetone, ammonia, hydrazine, and KOH.[12]

Scheme 2.1. Lithium 2,2,6,6-tetramethylpiperidine-mediated metalations of arenes.

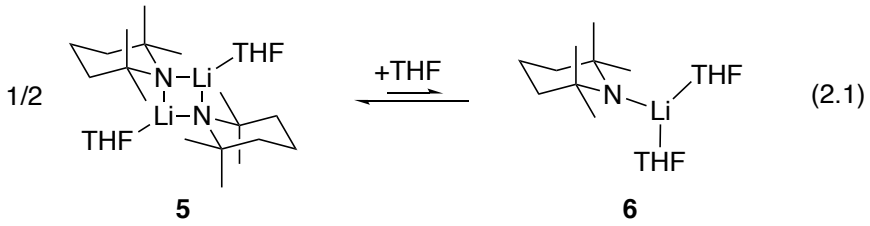


This paper describes our progress beyond the above analysis through the probing of a combination of selectivities and mechanisms of LiTMP-mediated ortholithiations. Although the

selectivities are largely founded in prior art,[13] only one detailed rate and mechanistic study of an LiTMP-mediated reaction—an epoxide elimination—has been reported.[14,15] We surveyed more than 40 arene metalations and selected arenes **1**–**4** (Scheme 2.1) for detailed study.

Results

Spectroscopic studies have shown that LiTMP is a 10:1 mixture of dimer **5** and monomer **6** in neat THF and >99:1 dimer at <1.3 M THF–hexane (eq 2.1).[16] The dimer–monomer solvation states were first studied with modified neglect of atomic overlap calculations[17] and later augmented with density functional theory (DFT) computations.[18,19] To simplify the presentation, we use the following shorthand: A = LiTMP subunit; S = THF; ArH = arene; ArLi = aryllithium. For example, A_2S_4 is a tetrasolvated dimer and $[A_2S_4(ArH)]^{‡}$ is the corresponding tetrasolvated-dimer-based transition structure.



5 **6**

Kinetics: General Protocol.[20] LiTMP was held in excess at standard concentrations (0.025–0.25 M). THF was also used in high but variable concentrations (2.6–12.2 M) with hexane as a cosolvent. Arenes were the limiting reagents (0.0025–0.010 M). Metalation rates were monitored using in situ IR spectroscopy by following the loss of strong arene absorbances in the range of 1323–1655 cm^{-1}. The time-dependent decays fit the first-order function $f(x) = ae^{-bx}$ such that b corresponds to the pseudo-first-order rate constant k_{obsd}. Values of k_{obsd} were shown to be independent of initial arene concentration as required for a first-order dependence. On occasion, initial rates were used if the LiTMP/ArH proportions deviated from pseudo-first order. All metalations displayed large isotope effects ($k_{obsd(H)}/k_{obsd(D)}$ = 23–40), which confirmed rate-limiting proton transfers. Large isotope effects in orthometalations, which can be evidence

of contributions from tunneling, were commonplace.[20a] A standard control experiment excluded the intervention of autocatalysis.[20b] After a first-order decay, the baseline was reestablished, and a second aliquot of arene was injected; the two rate constants were indistinguishable.

The orders in THF were determined by monitoring k_{obsd} versus THF concentration using hexane as the cosolvent. Similarly, plots of k_{obsd} versus LiTMP concentration afforded orders in LiTMP. The LiTMP dimer–monomer equilibrium in eq 2.1 presents added mathematical complexity to attaining rigorous fitting of THF and LiTMP concentration dependencies. We routinely cite orders stemming from fits to a simple power function ($y = ax^n$). The fits shown graphically, by contrast, are more rigorous and complex, as described below.

To account for the shift in ground state from dimer (A_2S_2) to monomer (AS_2), we must solve for the monomer and dimer concentration dependencies as a function of the equilibrium constant (K_{eq}), total base concentration ([A_{total}]), and total solvent concentration ([S]). Solving the system of two equations (eq 2.2 and 2.3) provides two sets of roots. We chose the sets corresponding to real, positive concentrations.

$$K_{eq} = \frac{\left[AS_2\right]^2}{\left[A_2S_2\right]\left[S\right]^2} \tag{2.2}$$

$$\left[A_{total}\right] = 2\left[A_2S_2\right] + \left[AS_2\right] \tag{2.3}$$

$$\left[A_2S_2\right] = \frac{1}{8}\left(4\left[A_{total}\right] + K_{eq}\left[S\right]^2 - \sqrt{K_{eq}}\left[S\right]\sqrt{8\left[A_{total}\right] + K_{eq}\left[S\right]^2}\right) \tag{2.4}$$

The choice of species (A_2S_2 versus AS_2) for writing rate expressions is arbitrary: A_2S_2 was chosen because of its dominance across the accessible THF concentration range (*vide infra*). Eq 2.4 describes the concentration of A_2S_2. In the discussion, we return to the challenges posed by two or more observable reactants with concentrations that vary with reaction conditions.

1,4-*bis*-(trifluoromethyl)benzene (1). A plot of k_{obsd} versus THF concentration (Figure 2.1) for the metalation of **1** to form **1-Li** shows a clean second-order dependence, $n = 2.02 \pm 0.07$ when fit to a simple power function, although a rigorous fit is more complex (*vide infra*). A plot of k_{obsd} versus LiTMP concentration at a 6.0 M THF concentration (Figure 2.2) shows an approximate first-order dependence. (Origins of the slight downward curvature are discussed in detail below.) When these results are taken together, the idealized rate law[21] in eq 2.5 is consistent with the generic mechanism shown in eq 2.6.

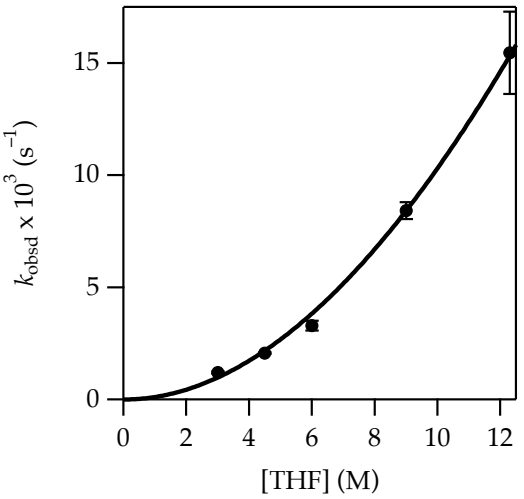


Figure 2.1. Plot of k_{obsd} vs tetrahydrofuran (THF) concentration for the metalation of **1** (0.010 M) at –78 °C measured with IR spectroscopy (1323 cm^{-1}). The curve depicts an unweighted least-squares fit to eq 2.5 that accounts for the shifting dimer–monomer mixtures described by eq 2.4. A simple fit to $y = ax^n$ affords $a = 0.10 \pm 0.02$, $n = 2.02 \pm 0.07$.

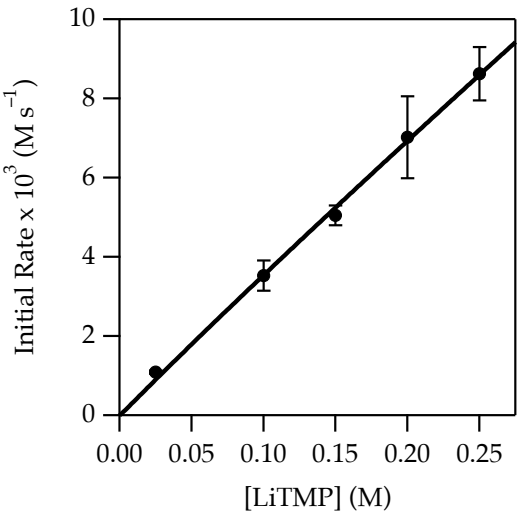


Figure 2.2. Plot of initial rate vs lithium 2,2,6,6-tetramethylpiperidine (LiTMP) concentration for the metalation of **1** (0.010 M) in 6.0 M THF/hexane at –78 °C measured with IR spectroscopy (1323 cm^{-1}). The curve depicts an unweighted least-squares fit to eq 2.5 that accounts for the shifting dimer–monomer mixtures described by eq 2.4. A simple fit to $y = ax^n$ affords $a = 33.07 \pm 2.19$, $n = 0.97 \pm 0.04$.

$$d[ArLi]/dt = k[ArH]^1[S]^2[A_2S_2]^1 \qquad (2.5)$$

$$\underset{\mathbf{1}}{A_2S_2} + 2S \underset{}{\overset{K_{eq}}{\rightleftharpoons}} \underset{\mathbf{7}}{[A_2S_4]} \xrightarrow{k[ArH]} \underset{\mathbf{1\text{-}Li}}{ArLi} \qquad (2.6)$$

Owing to the severe steric hindrance of an A_2S_4 cyclic dimer[15–18] as a reactant or a transition structure, the rate data implicate triple ions.[22] Such LiTMP-derived triple ions have been structurally characterized[23] and studied computationally.[17]

1,3-*bis*-(trifluoromethyl)benzene (2). The metalation of **2** at –78 °C affords exclusively the 4-lithiated product **2-Li** as shown by deuteration. Fitting the THF dependence to a simple power function shows an intermediate order of 1.50 ± 0.04 (Figure 2.3), which suggests at least two mechanisms at play. Similarly, the measured LiTMP order fit to a power function is 0.76 ±

0.04 (Figure 2.4), which attests to competing monomer- and dimer-based metalations. The fits in Figures 2.3 and 2.4 are consistent with the idealized rate law in eq 2.7 and the mechanisms shown in eqs 2.8 and 2.9.[24]

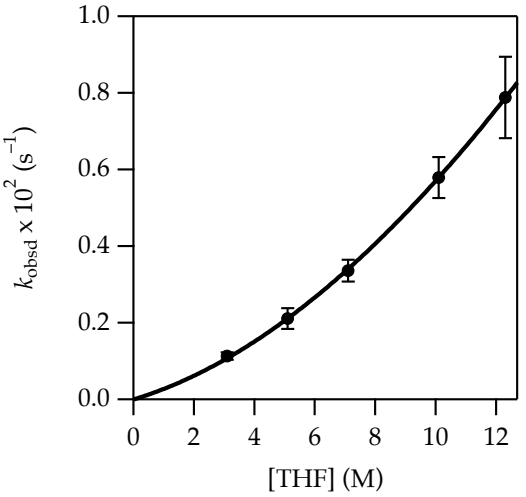


Figure 2.3. Plot of k_{obsd} vs THF concentration for the metalation of **2** (0.0025 M) at –78 °C measured with IR spectroscopy (1356 cm^{-1}). The curve depicts an unweighted least-squares fit to eq 2.7 that accounts for the shifting dimer–monomer mixtures described by eq 2.4. A simple fit to $y = ax^n$ affords $a = 0.018 \pm 0.002$, $n = 1.50 \pm 0.04$.

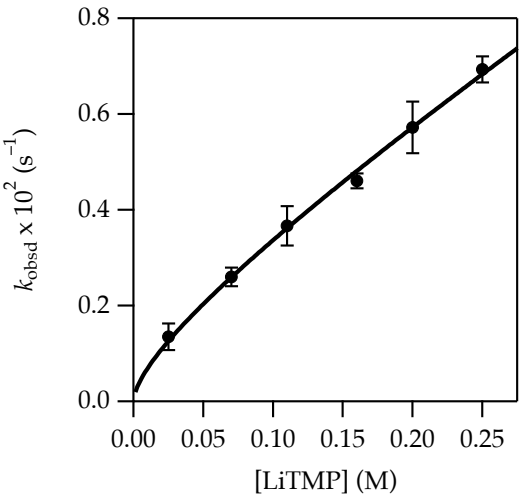


Figure 2.4. Plot of k_{obsd} vs LiTMP concentration for the metalation of **2** (0.0025 M) in 6.0 M THF/hexane at –78 °C measured with IR spectroscopy (1356 cm^{-1}). The curve depicts an unweighted least-squares fit to eq 2.7 that accounts for the shifting dimer–monomer mixtures described by eq 2.4. A simple fit to $y = ax^n$ affords $a = 1.9 \pm 0.1$, $n = 0.76 \pm 0.04$.

$$d[ArLi]/dt = k_1[ArH]^1[S]^1[A_2S_2]^{1/2} + k_2[ArH]^1[S]^2[A_2S_2]^1 \qquad (2.7)$$

$$\underset{\mathbf{5}}{1/2A_2S_2} + S \underset{}{\overset{K_{eq}}{\rightleftharpoons}} \underset{\mathbf{6}}{AS_2} \xrightarrow{k_1[ArH]} \underset{\mathbf{2\text{-}Li}}{ArLi} \qquad (2.8)$$

$$\underset{\mathbf{5}}{A_2S_2} + 2S \underset{}{\overset{K_{eq}}{\rightleftharpoons}} \underset{\mathbf{7}}{[A_2S_4]} \xrightarrow{k_2[ArH]} \underset{\mathbf{2\text{-}Li}}{ArLi} \qquad (2.9)$$

Kinetics: 1,3-*bis*-(Methoxy)benzene (3). The metalation of **3** at –40 °C to form **3-Li** shows a clean first-order THF dependence (Figure 2.5) and half-order LiTMP dependence (Figure 2.6) when fit to a simple power function. The results are consistent with exclusively disolvated-monomer-based metalation (eqs 2.10 and 2.11). We explain below *why* the data fit power functions well despite measurable shifts in LiTMP structure.

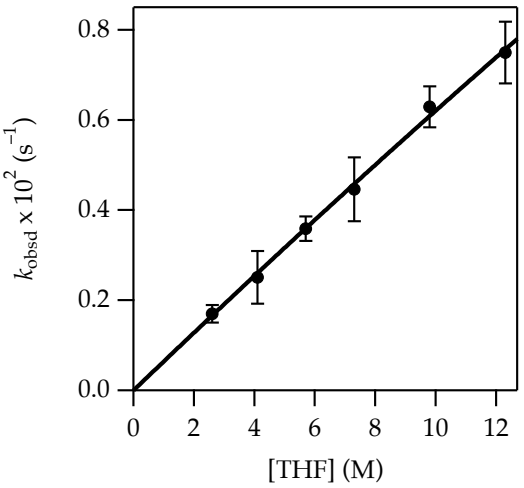


Figure 2.5. Plot of k_{obsd} vs THF concentration for the metalation of **3** (0.0025 M) at –40 °C measured with IR spectroscopy (1496 cm^{-1}). The curve depicts an unweighted least-squares fit to eq 2.10 that accounts for the shifting dimer–monomer mixtures described by eq 2.4. A simple fit to $y = ax^n$ affords $a = 0.065 \pm 0.005$, $n = 0.98 \pm 0.03$.

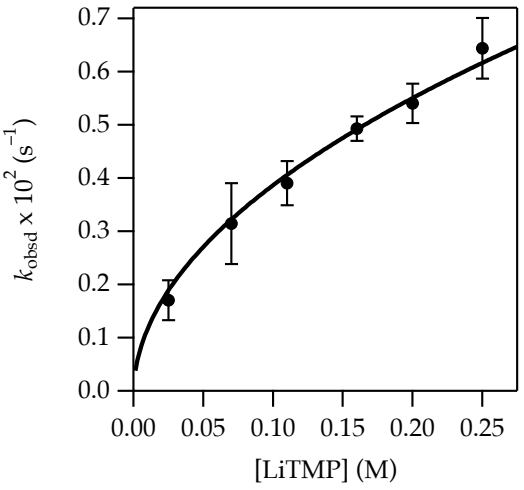


Figure 2.6. Plot of k_{obsd} vs LiTMP concentration for the metalation of **3** (0.0025 M) in 6.0 M THF/hexane at –40 °C measured with IR spectroscopy (1496 cm^{-1}). The curve depicts an

unweighted least-squares fit to eq 2.10 that accounts for the shifting dimer–monomer mixtures described by eq 2.4. A simple fit to $y = ax^n$ affords $a = 1.39 \pm 0.05$, $n = 0.57 \pm 0.02$.

$$d[ArLi]/dt = k[ArH]^1[S]^1[A_2S_2]^{1/2} \quad (2.10)$$

$$\underset{\mathbf{5}}{1/2A_2S_2} + S \overset{K_{eq}}{\rightleftharpoons} \underset{\mathbf{6}}{AS_2} \xrightarrow{k[ArH]} \underset{\mathbf{3\text{-}Li}}{ArLi} \quad (2.11)$$

Kinetics: 4,4-Dimethyl-2-phenyl-2-oxazoline (4). The metalation of **4** to form **4-Li** at –40 °C shows a zeroth-order THF dependence (Figure 2.7). The slight downward drift is too small to be relevant, particularly given subtle secondary-shell effects of similar magnitude;[20] however, there is a subtle and pedagogical reason why it *should* be observable. The THF dependence in conjunction with a half-order LiTMP dependence (Figure 2.8) is consistent with the monosolvated-monomer-based mechanism (eqs 2.12 and 2.13).

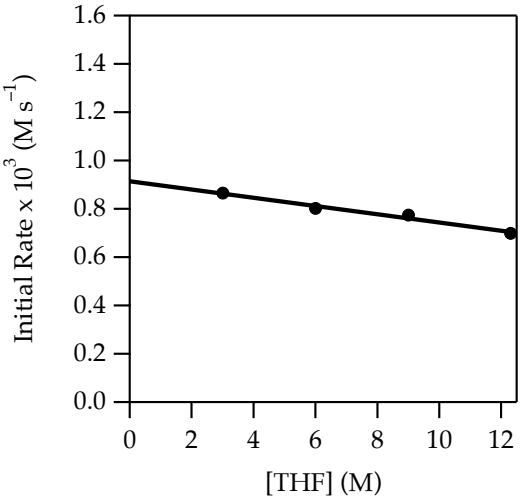


Figure 2.7. Plot of initial rate vs THF concentration in hexane for the metalation of **4** (0.010 M) at –40 °C measured with IR spectroscopy (1655 cm^{-1}). The curve depicts an unweighted least-squares fit to $y = ax + b$ ($a = 0.91 \pm 0.02$, $b = -0.017 \pm 0.002$).

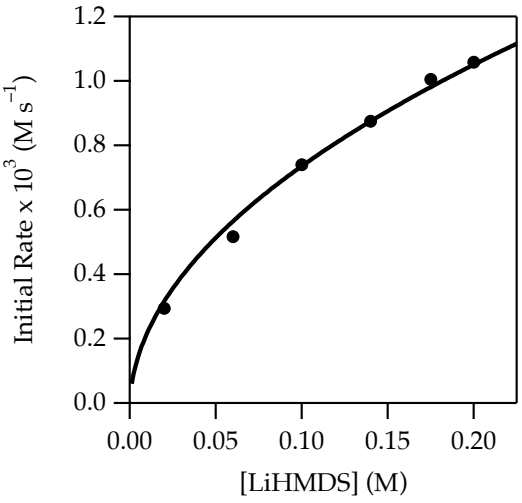


Figure 2.8. Plot of initial rate vs LiTMP concentration in hexane for the metalation of **4** (0.010 M) at –40 °C measured with IR spectroscopy (1655 cm^{-1}). The curve depicts an unweighted least-squares fit to eq 2.12 that accounts for the shifting dimer–monomer mixtures described by eq 2.4. A simple fit to $y = ax^n$ affords $a = 2.7 \pm 0.1$, $n = 0.57 \pm 0.02$.

$$d[ArLi]/dt = k[ArH]^1[S]^0[A_2S_2]^{1/2} \qquad (2.12)$$

$$\underset{\textbf{5}}{1/2A_2S_2} \overset{K_{eq}}{\rightleftharpoons} \underset{\textbf{6}}{[AS]} \xrightarrow{k[ArH]} \underset{\textbf{4-Li}}{ArLi} \qquad (2.13)$$

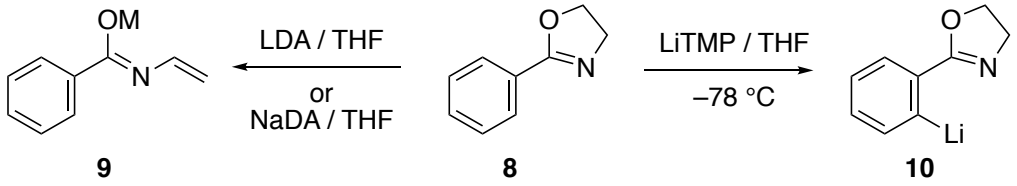
Discussion

Qualitative Observations. The work described herein focuses on rate studies of four LiTMP-mediated orthometalations. It is instructive, however, to qualitatively compare LiTMP with LDA as well as with sodium diisopropylamide (NaDA) based on the results of a preliminary survey of approximately 40 arene metalations carried out to choose appropriate substrates for study. Thermochemically recalcitrant metalations such as arene **3** metalate incompletely *at equilibrium* using excess LDA and NaDA, whereas metalations by LiTMP are

generally quantitative.[25,26] However, stoichiometric LiTMP also affords an incomplete metalation of **3** at equilibrium, putting the relative thermochemical boost by LiTMP in the vicinity of an order of magnitude (a single pK_A unit), consistent with the results of Fraser and co-workers.[7] Comparing and contrasting the metalation rates shows that reactions with LiTMP are 5–500 times faster than those with LDA under comparable conditions for the few substrates slow enough to be monitored. By contrast, metalation rates for LiTMP and NaDA tend to be comparable.[26]

The regioselectivities of LiTMP are distinct from those of either LDA or NaDA. The hindered TMP fragment has two effects: (1) LiTMP metalates less acidic but sterically more accessible sites,[4] such as the 4 position of **2** to give **2-Li**; and (2) the product TMPH does not mediate regiochemical equilibration to the more acidic sites.[10] Previous studies of arene metalations using LDA showed facile equilibration from kinetic to thermodynamic products in the presence of free diisopropylamine: the metalations are reversible.[12] We submit that many reported regioselectivities lack sufficient controls with which to ascertain whether the regioselectivity is the result of kinetic or thermodynamic control.

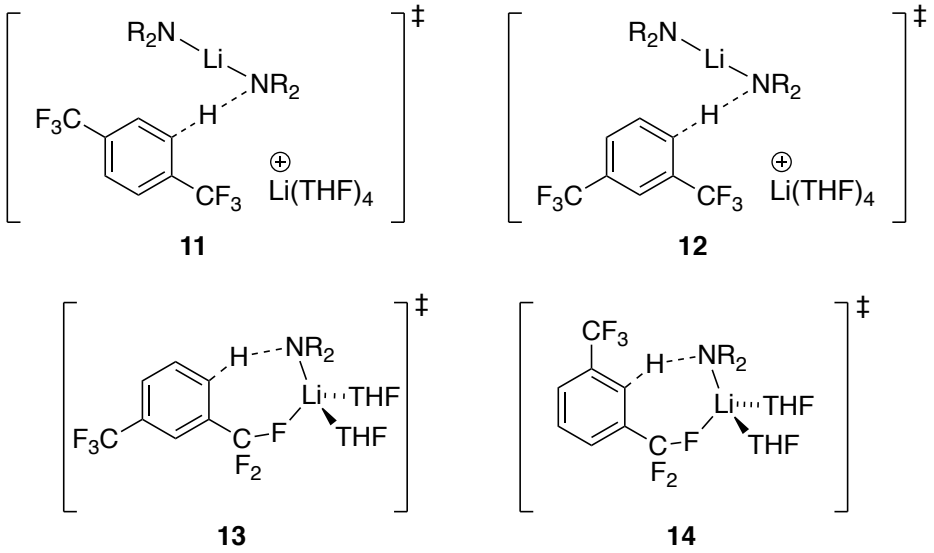
Contrary to our earlier report,[27] the metalation of **8** lacking the protective gem-dimethyl moiety of **4** by LDA results in decomposition consistent with the formation of **9** rather than the reported orthometalated product **10** (eq 2.14).[26] Similar decomposition is obtained with NaDA.[26] By contrast, the LiTMP-mediated ortholithiation of **8** affords **10**, as shown by deuterium quenching along with limited (15%) decomposition.



(2.14)

Mechanism of Ortholithiation. Orthometalation of the four substrates reveals a substrate-dependent mix of mechanisms. Arene **1**,[13a] which has para-disposed CF_3 moieties,

proceeds via a transition structure of stoichiometry $[A_2S_4(ArH)]^‡$. The high solvation numbers are incompatible with any form of cyclic- or open-dimer-based metalation and instead suggest that the role of triple ion **11** is analogous to those invoked in a number of previous investigations.[20,22,23] DFT computations suggest a weak dipolar interaction between a fluorine and the lithium cation owing to minor distortion that does not rise to the level of a discrete contact.



Notably, 1,3-bis(trifluoromethyl)benzene (**2**)[13b] metalates at the external C-4 position with no tendency to equilibrate to the C-2 position. Adding diisopropylamine causes complete equilibration to the 2-lithiated isomer, which confirms that the regioselectivity is under kinetic control. Rate studies reveal a composite of an $[A_2S_4(ArH)]^‡$ dimer-based metalation along with $[AS_2(ArH)]^‡$ monomer-based metalation consistent with computed transition structures **12** and **13**, respectively. DFT computations indicate that metalation at C-2 via **14** is a barrier +2.0 kcal/mol higher barrier than that via **13**, consistent with experiment.

1,3-Dimethoxybenzene (**3**) metalates exclusively at the internal (doubly ortho) C-2 position.[13c] Rate studies showed only an $[AS_2(ArH)]^‡$ monomer-based pathway. DFT

computations showed a 2.1 Å MeO–Li interaction (**15**) and affiliated near-tetrahedral lithium coordination sphere (Figure 2.9). Compared with those of **15**, computations of the AS_2-mediated external metalation (**16**) also manifested a MeO–Li interaction and a +2.6 kcal/mol higher energy consistent with experiment.

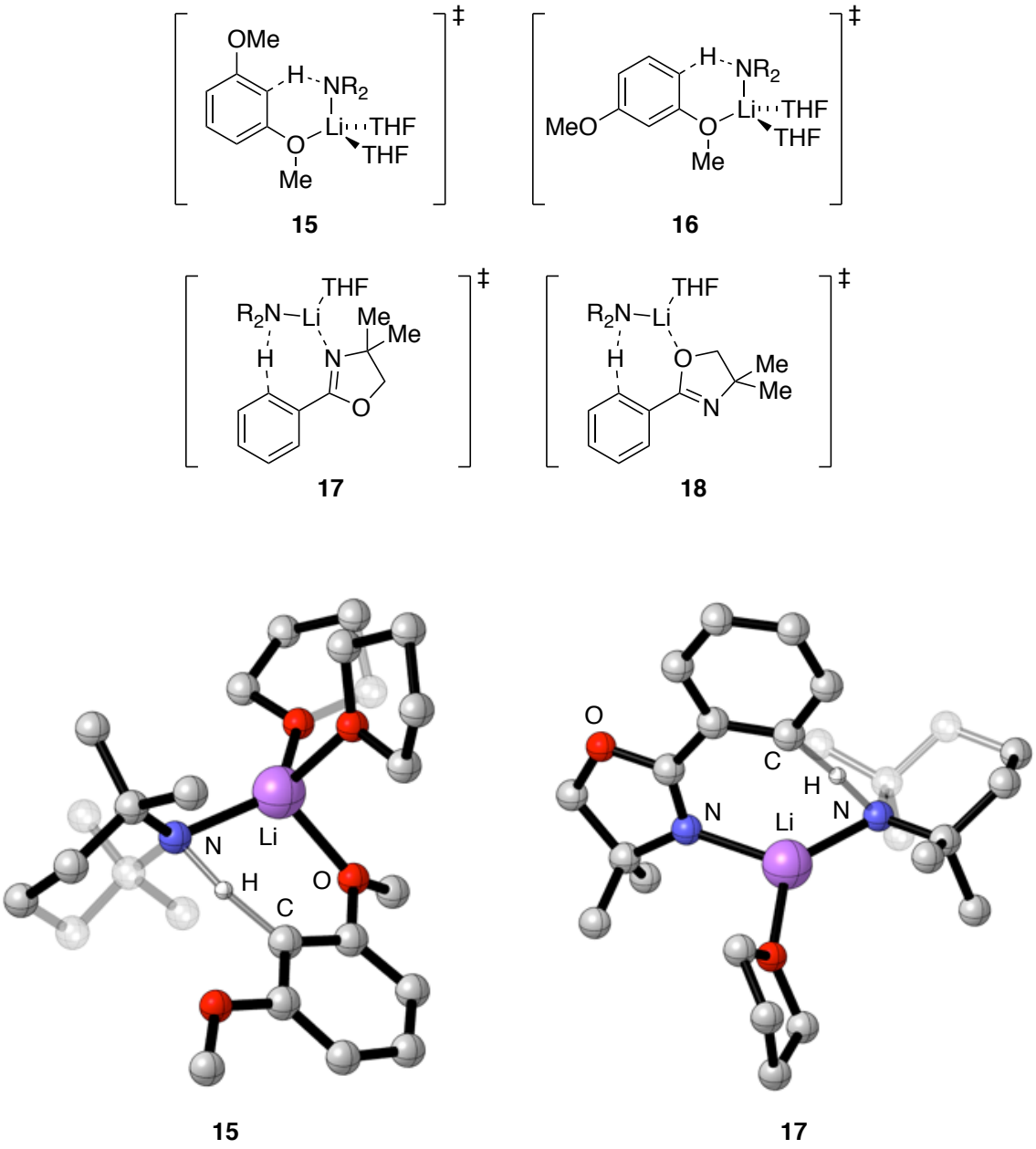


Figure 2.9. Ball-and-stick representation of transition structures **15** and **17**.

Lithiation of oxazoline **4** proceeds via an [AS(ArH)]‡ monosolvated monomer (**17**).[13d] Previous studies have all supported N–Li versus O–Li interaction at the transition structure.[28] Indeed, N-bound transition structure **17** is 4.4 kcal/mol more stable than the O-bound isomer **18**. On first inspection, the computed preference along with a seemingly modest threefold reduction in metalation rate compared with that of **8** (eq 2.14) may seem odd given the apparent steric demands of the methyl moieties. However, the methyl moieties in transition structure **17** seem to add no significant congestion.

Consequence of a Shifting Ground State. Organolithium mechanistic studies often present the complexity of either mixtures of reactants or multiple competing pathways (rate-limiting transition structures.) The latter is a relatively simple kinetic problem of deconvoluting the relative contributions of a multi-term rate law.[20a] Condition-dependent changes in reactants, by contrast, are far more challenging, historically prompting us to simply avoid them. Only recently did we begin to understand the challenges of the influence of multiple reactants on observable rate behavior.[29]

At the outset of the present study, we surmised that a shift in the observable form of LiTMP from purely disolvated dimer (2.0–9.0 M THF/hexane) to a 90/10 mixture of disolvated dimer and disolvated monomer in neat THF (eq 2.1) would have a significant (≈10%) impact on the measured reaction order in LiTMP. That hypothesis proved only partly correct. Consider the simplest depiction of a monomer-based metalation (devoid of solvents) in eq 2.15. In the limit that dimer "A_2" is the sole observable form, a fit to the simple power function $y = a[A_{total}]^n$ would show a clean half-order dependence (n = 0.50). Conversely, exclusively observable monomer "A" would afford a first-order LiTMP dependence (n = 1.0). We posed this question: what is the effect of a dimer-monomer mixture on the measured LiTMP order? A plot of measured order ascertained from the simple power function versus percent observable monomer is shown in Figure 2.10. We hasten to add that we use *normality* rather than molarity (50% monomer would be a 1:1 integration in the ^{6}Li NMR spectrum).

$$1/2\ A_2 \underset{}{\overset{K_{eq}}{\rightleftharpoons}} A \longrightarrow [A]^{\ddagger} \qquad (2.15)$$

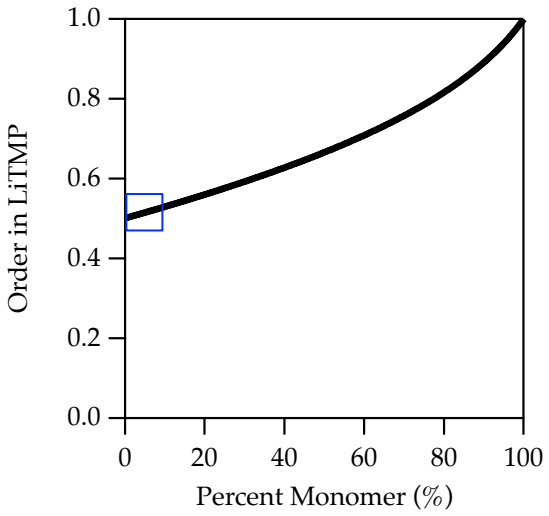


Figure 2.10. Simulated plot of LiTMP order as a function of percent monomer (measured using normality, N). The blue box represents the range accessible to 0.10 N LiTMP in THF/hexane mixtures at –78 °C (eq 2.1).

The blue box in Figure 2.10 shows the dimer–monomer concentration range observed for LiTMP from nearly neat hexane to neat THF. The presence of 10% monomer has an insignificant effect on the measured order (n = 0.53). We confess to being a bit surprised. By contrast, owing to the nonlinearity, the perturbation of the measured order when observable monomer is contaminated by 10% dimer is more significant (n = 0.82).

This point in the discussion seems to be an opportune time to mention another misunderstood concept about how deaggregation influences reactivity. First, that monomers are more reactive than dimers is by no means a foregone conclusion; this anachronistic thinking derives from rate studies of polymerizations during the 1960s and 1970s.[30] Aggregates often react preferentially.[13c,14,20,23a,31] Second, even if a monomer is the preferred reactive form,

changes in solvent or solvent concentration that force monomer formation will *not* necessarily increase the reaction rate (eq 2.16). If, for example, "AS" is the reactive form, driving the reactant to AS_2 by using a high solvent concentration will inhibit the metalation.[29]

$$1/2\ A_2S_2 \overset{K_{eq}}{\rightleftharpoons} [AS] \overset{K'_{eq}[S]}{\rightleftharpoons} AS_2 \qquad (2.16)$$

Conclusions

LiTMP offers advantages over alkyllithiums by being less nucleophilic—more functional-group-compatible—and over LDA with respect to both the metalation rate and steric-based regiocontrol. The absence of amine-mediated equilibration ensures kinetic control of the regioselectivity except when ArH–ArLi direct exchanges are possible.[11] Cost, the primary limitation, appears to us to be artificial and is certainly so on a scale at which competitive pricing should be available. The functional-group-dependent mechanisms—$[A_2S_4(ArH)]^‡$, $[AS_2(ArH)]^‡$, and $[AS(ArH)]^‡$—determined from a survey of only four substrates representing only two functionalities (MeO and CF_3) suggest that careful control of conditions, particularly coordinating solvent and solvent concentration,[20a] offers the potential for often overlooked regiocontrol. For the more mechanistically minded, the progress made in addressing mechanisms in which multiple species are observable reactants is notable and remains one of the more serious challenges for exploring complex ensembles.

Experimental

Reagents and Solvents. THF and *n*-hexane were distilled from solutions containing sodium benzophenone ketyl. LiTMP, [^{6}Li]LiTMP, and [^{6}Li,^{15}N]LiTMP were prepared as described previously.[16a] Air- and moisture-sensitive materials were manipulated under argon using standard glove box, vacuum line, and syringe techniques. The arenes were purchased from Sigma Aldrich.

NMR Spectroscopy. All NMR samples for reaction monitoring and structure elucidation were prepared using stock solutions and sealed under partial vacuum as described in detail previously.[9k,20b] Standard ^{1}H, ^{6}Li, ^{13}C, and ^{15}N NMR spectra were recorded at 500, 73.57, 125.79, and 36.14 MHz, respectively.

IR Spectroscopy. IR spectra were recorded using an in situ IR spectrometer fitted with a 30-bounce, silicon-tipped probe. The spectra were acquired in 16 scans at a gain of 1 and a resolution of 4 cm^{-1}. A representative reaction was carried out as follows: The IR probe was inserted through a nylon adapter and O-ring seal into an oven-dried, cylindrical flask fitted with a magnetic stir bar and a T-joint. The T-joint was capped with a septum for injections and a nitrogen line. After evacuation under full vacuum, heating, and flushing with nitrogen, the flask was charged with LiTMP (73.6 mg, 0.50 mmol) in THF/hexane (4.9 mL total volume) and cooled to –78 °C with a dry ice/acetone bath. After a background spectrum was recorded, arene **1** was added (0.050 mmol in 0.10 mL) with stirring. The absorbance at 1323 cm^{-1} was monitored over the course of the reaction.

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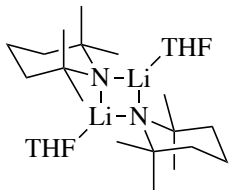
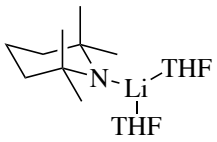
I. NMR Spectroscopic Studies

Table A.2.1. ^{6}Li NMR chemical shifts and coupling constants for the different species in neat THF at –80 °C.

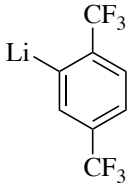
Species	δ (ppm)	$J_{Li\text{-}N}$ (Hz)
A_2S_2	1.51	4.8
AS_2	0.90	8.9
1-Li	0.88	–
2-Li	0.84	–
3-Li Mixed Aggregate	2.19	5.1
4-Li Mixed Aggregate	2.11	5.1



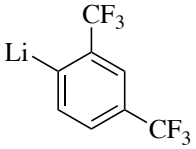
A_2S_2



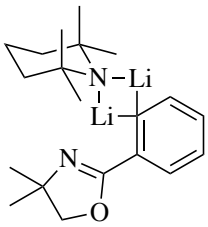
AS_3



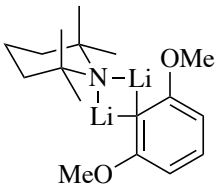
1-Li



2-Li



3-Li
Mixed Aggregate



4-Li
Mixed Aggregate

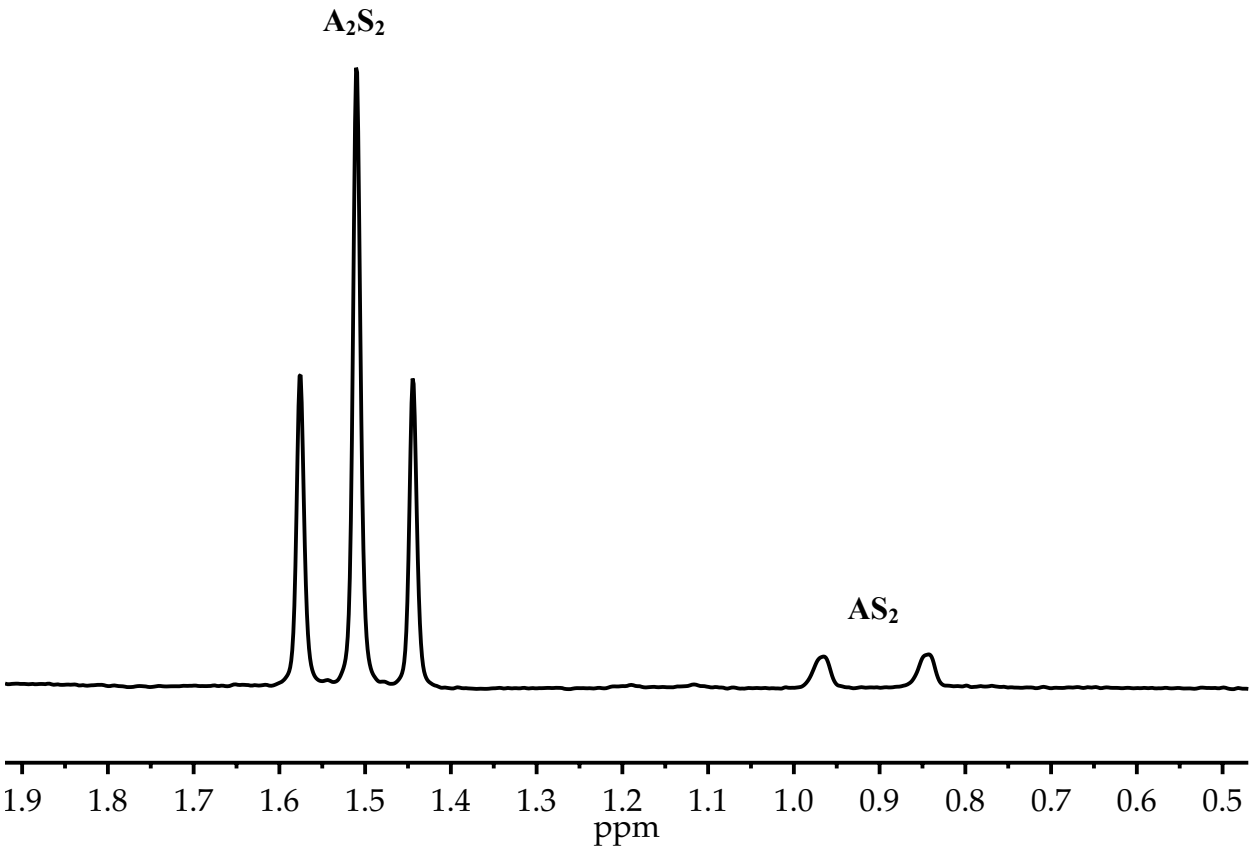


Figure A.2.1. ^{6}Li spectrum of 0.10 M [^{6}Li,^{15}N]LiTMP in neat THF at –80 °C.

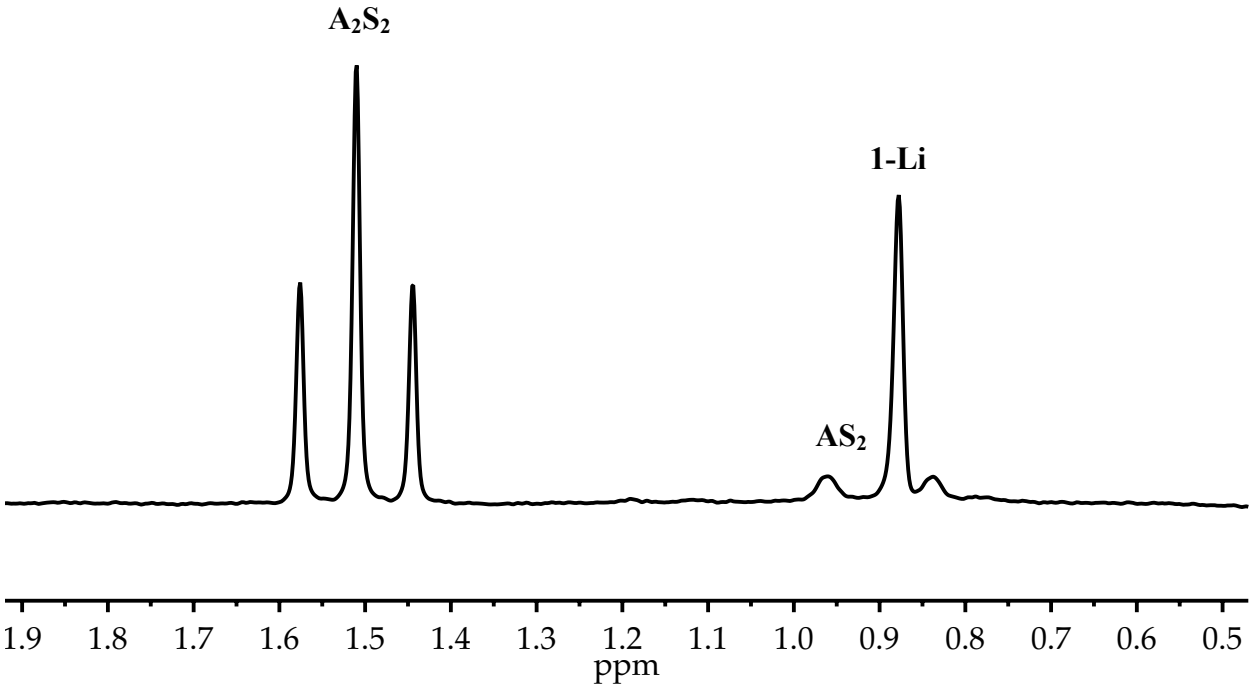


Figure A.2.2. ^{6}Li spectrum of 0.10 M [^{6}Li,^{15}N]LiTMP and 0.030 M **1** in neat THF at –80 °C after aging at –80 °C for 2 h. The lithiated product (**1-Li**) shows no mixed aggregation with free LiTMP as evidenced by the singlet.

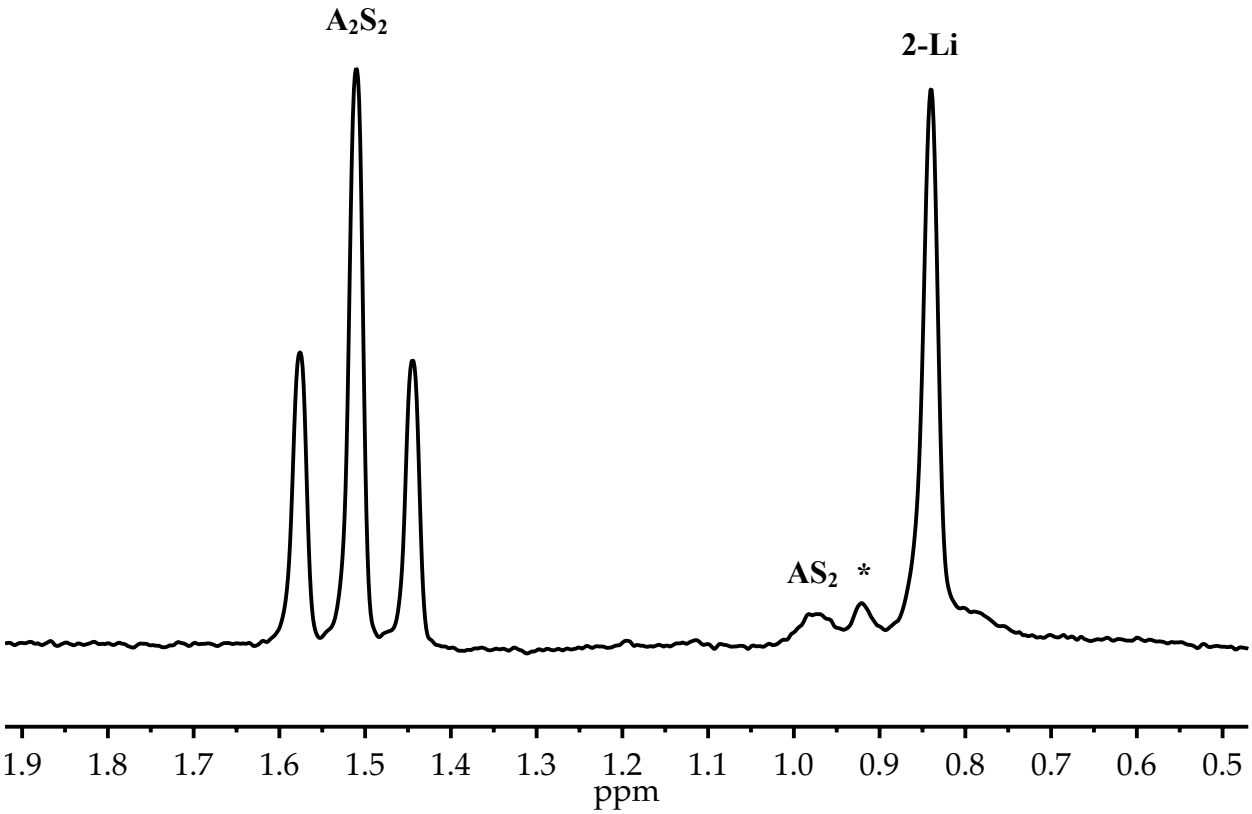


Figure A.2.3. ^{6}Li spectrum of 0.10 M [^{6}Li,^{15}N]LiTMP and 0.030 M **2** in neat THF at –80 °C after aging at –80 °C for 2 h. The lithiated product (**2-Li**) shows no mixed aggregation with free LiTMP as evidenced by the singlet. (Note: the * indicates a minor contribution of the internally metalated product.)

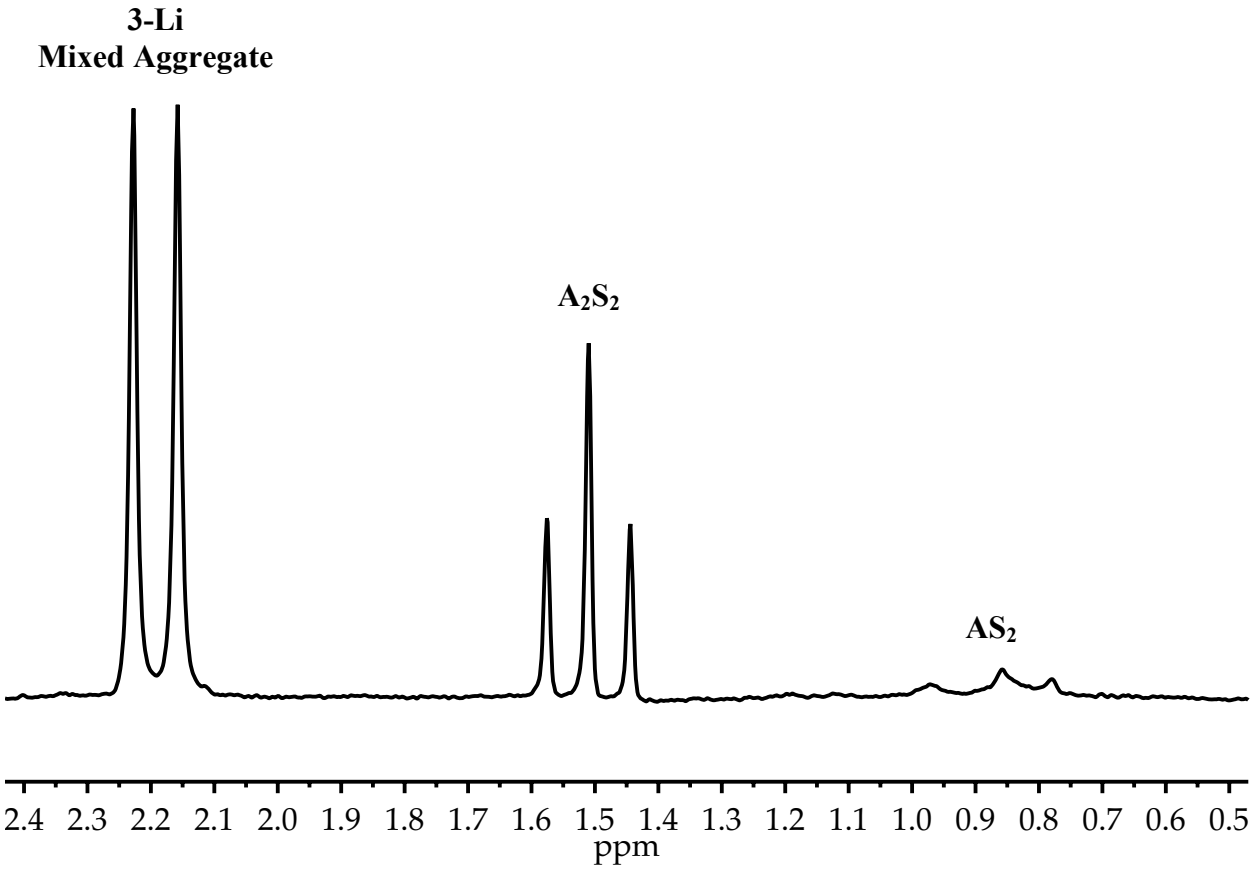


Figure A.2.4 ^{6}Li spectrum of 0.10 M [^{6}Li,^{15}N]LiTMP and 0.030 M **3** in neat THF at –80 °C after aging at –40 °C for 2 h. The lithiated product (**3-Li**) forms a dimeric mixed aggregate with free LiTMP as evidenced by the doublet and coupling constant.

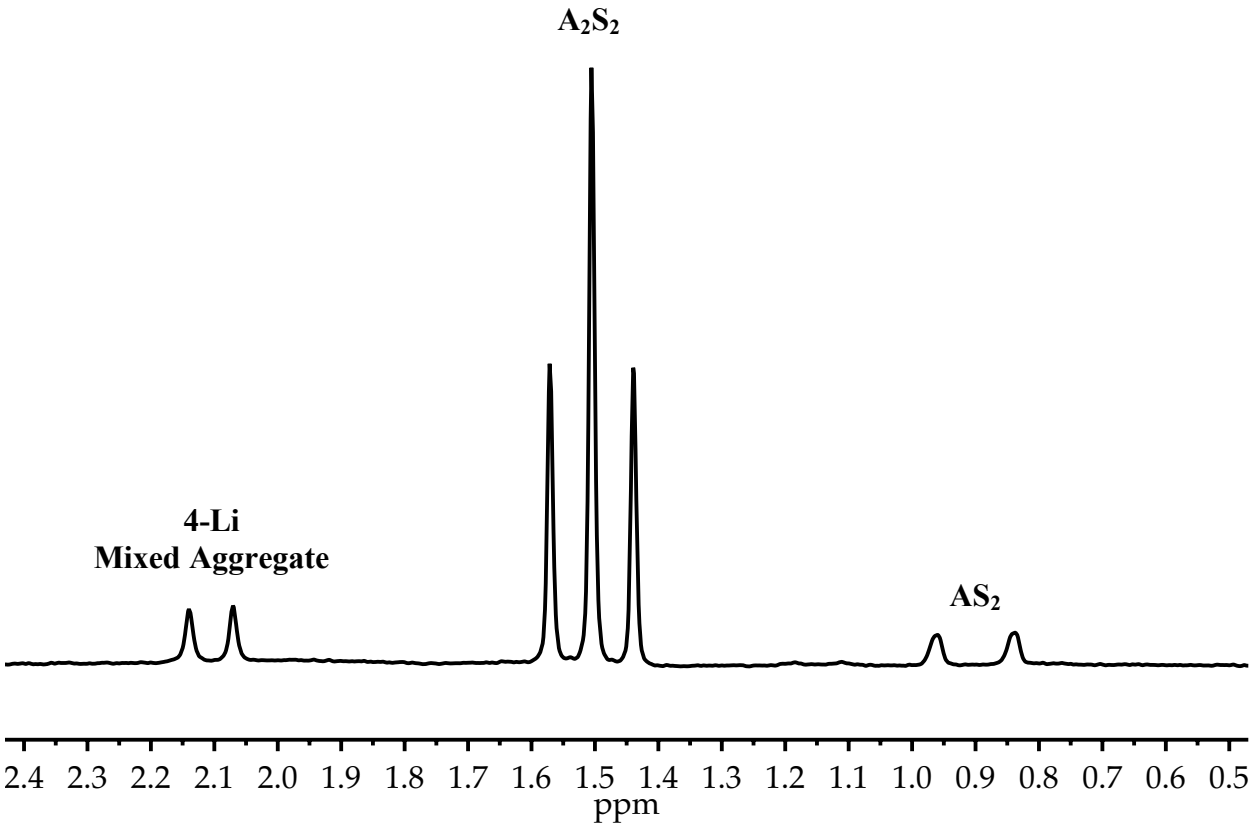
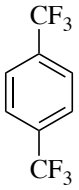


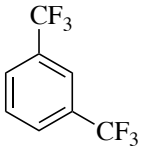
Figure A.2.5. ^{6}Li spectrum of 0.10 M [^{6}Li,^{15}N]LiTMP and 0.030 M **4** in neat THF at –80 °C after aging at –40 °C for 2 h. The lithiated product (**4-Li**) forms a dimeric mixed aggregate with free LiTMP as evidenced by the doublet and coupling constant.

II. IR Rate Studies

Chart A.2.1. Substrates for Orthometalations



1



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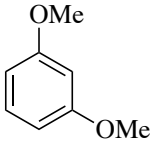

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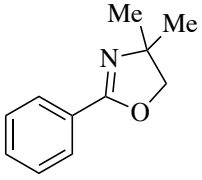

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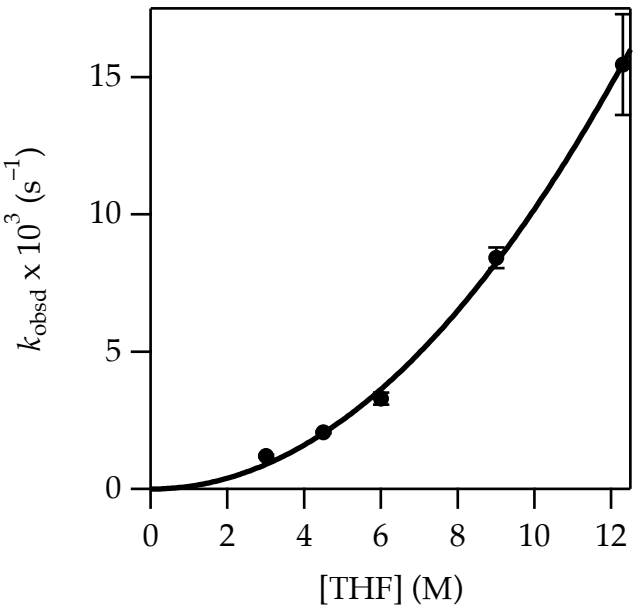


Figure A.2.6. Plot of k_{obsd} vs. THF concentration in hexane for the metalation of **1** (0.010 M) by LiTMP (0.10 M) at –78 °C measured with IR spectroscopy (1323 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 0.10 \pm 0.02$, $n = 2.02 \pm 0.07$).

[THF] (M)	$k_{obsd}^1 \times 10^3$ (s^{-1})	$k_{obsd}^2 \times 10^3$ (s^{-1})	$k_{obsd}^{avg} \times 10^3$ (s^{-1})
3.0	1.2349	1.1623	1.20 ± 0.05
4.5	2.0881	2.0391	2.06 ± 0.03
6.0	3.4505	3.1484	3.3 ± 0.2
9.0	8.1481	8.6858	8.4 ± 0.4
12.3	14.1630	16.7650	15 ± 2

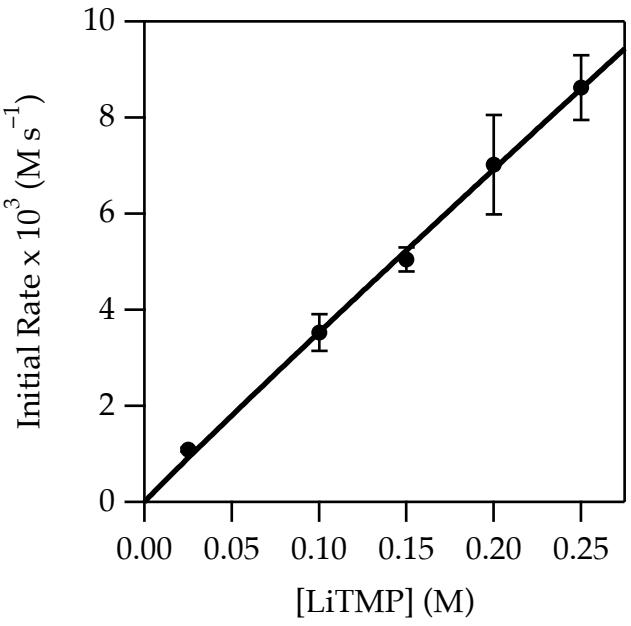


Figure A.2.7. Plot of initial rate vs. LiTMP concentration in 6.0 M THF with hexane cosolvent for the metalation of **1** (0.010 M) at –78 °C measured with IR spectroscopy (1323 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 33.07 \pm 2.19$, $n = 0.97 \pm 0.04$).

[LiTMP] (M)	Initial Rate[1] × 10^3 ($M\ s^{-1}$)	Initial Rate[2] × 10^3 ($M\ s^{-1}$)	Initial Rate[avg] × 10^3 ($M\ s^{-1}$)
0.025	1.0611	1.1226	1.09 ± 0.04
0.10	3.2593	3.7978	3.5 ± 0.4
0.15	4.8724	5.2261	5.0 ± 0.3
0.20	6.2916	7.756	7 ± 1
0.25	8.1469	9.0975	8.6 ± 0.7

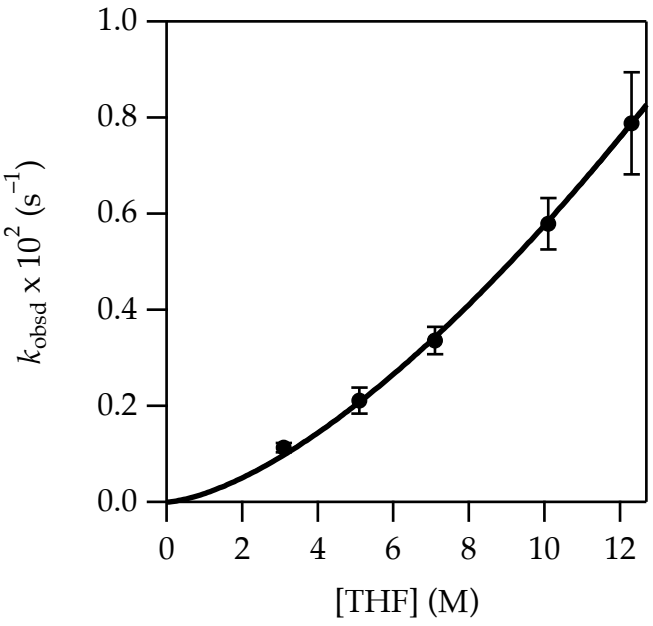


Figure A.2.8. Plot of k_{obsd} vs. THF concentration in hexane for the metalation of **2** (0.0025 M) by LiTMP (0.10 M) at –78 °C measured with IR spectroscopy (1356 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 0.018 \pm 0.002$, $n = 1.50 \pm 0.04$).

[THF] (M)	$k_{obsd}^{1} \times 10^2$ (s^{-1})	$k_{obsd}^{2} \times 10^2$ (s^{-1})	$k_{obsd}^{avg} \times 10^2$ (s^{-1})
3.0	0.10584	0.11988	0.11 ± 0.01
5.0	0.19222	0.23033	0.21 ± 0.03
7.0	0.35638	0.31640	0.34 ± 0.3
10.0	0.61657	0.54127	0.58 ± 0.5
12.3	0.86309	0.71293	0.8 ± 0.1

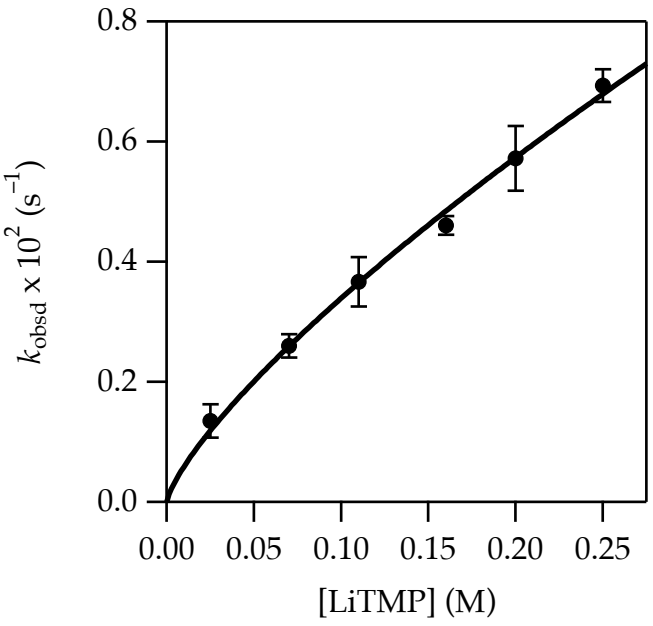


Figure A.2.9. Plot of k_{obsd} vs. LiTMP concentration in 6.0 M THF with hexane cosolvent for the metalation of **2** (0.0025 M) at –78 °C measured with IR spectroscopy (1356 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 1.9 \pm 0.1$, $n = 0.76 \pm 0.04$).

[THF] (M)	$k_{obsd}^{1} \times 10^2$ (s^{-1})	$k_{obsd}^{2} \times 10^2$ (s^{-1})	$k_{obsd}^{avg} \times 10^2$ (s^{-1})
0.025	0.11550	0.15455	0.14 ± 0.03
0.070	0.24632	0.27404	0.26 ± 0.02
0.11	0.33746	0.39563	0.37 ± 0.04
0.16	0.44992	0.47159	0.46 ± 0.02
0.20	0.61031	0.53383	0.57 ± 0.05
0.25	0.67421	0.71238	0.69 ± 0.03

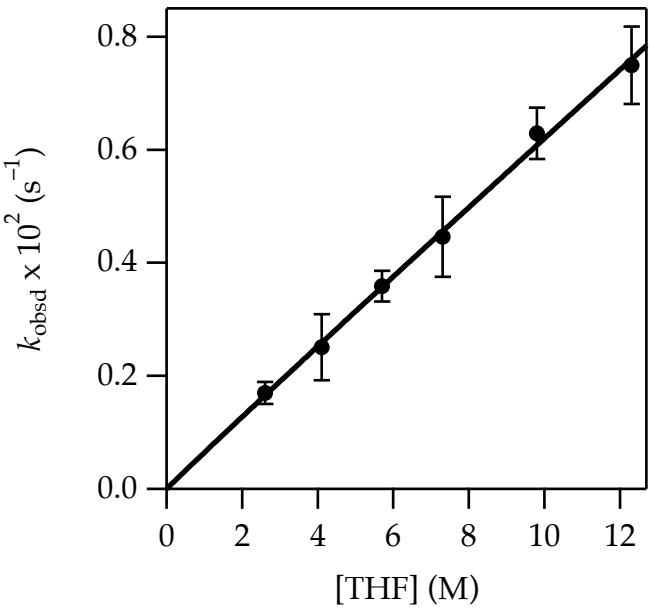


Figure A.2.10. Plot of k_{obsd} vs. THF concentration in hexane for the metalation of **3** (0.0025 M) by LiTMP (0.10 M) at –40 °C measured with IR spectroscopy (1496 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 0.065 \pm 0.005$, $n = 0.98 \pm 0.03$).

[THF] (M)	$k_{obsd}^{1} \times 10^2$ (s^{-1})	$k_{obsd}^{2} \times 10^2$ (s^{-1})	$k_{obsd}^{avg} \times 10^2$ (s^{-1})
2.5	0.18386	0.1563	0.17 ± 0.02
4.0	0.29205	0.20944	0.25 ± 0.06
5.6	0.33978	0.37821	0.36 ± 0.03
7.2	0.39605	0.49637	0.45 ± 0.07
9.7	0.59712	0.66112	0.63 ± 0.05
12.3	0.70152	0.79822	0.75 ± 0.07

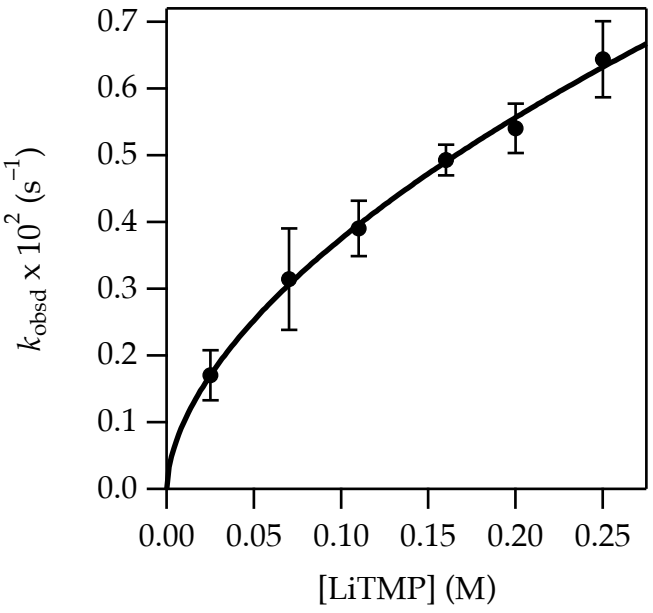


Figure A.2.11. Plot of k_{obsd} vs. LiTMP concentration in 6.0 M THF with hexane cosolvent for the metalation of **3** (0.0025 M) at –40 °C measured with IR spectroscopy (1496 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 1.39 \pm 0.05$, $n = 0.57 \pm 0.02$).

[THF] (M)	$k_{obsd}^{1} \times 10^2$ (s^{-1})	$k_{obsd}^{2} \times 10^2$ (s^{-1})	$k_{obsd}^{avg} \times 10^2$ (s^{-1})
0.025	0.19712	0.1438	0.17 ± 0.04
0.070	0.26101	0.36832	0.31 ± 0.08
0.11	0.4198	0.36122	0.39 ± 0.04
0.16	0.47688	0.50936	0.49 ± 0.02
0.20	0.56696	0.5143	0.54 ± 0.04
0.25	0.60363	0.68393	0.64 ± 0.06

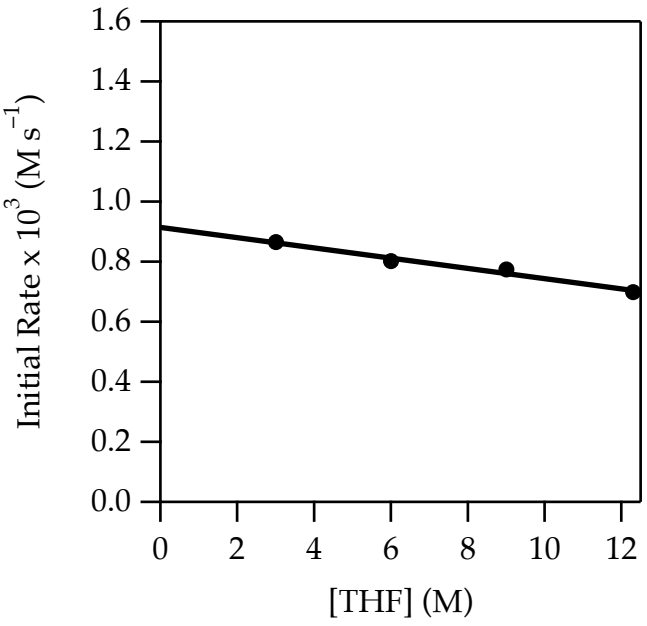


Figure A.2.12. Plot of k_{obsd} vs. THF concentration in hexane for the metalation of **4** (0.010 M) by LiTMP (0.10 M) at –40 °C measured with IR spectroscopy (1655 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax + b$ ($a = 0.91 \pm 0.02$, $b = -0.017 \pm 0.002$).

[THF] (M)	Initial Rate × 10^3 ($M\ s^{-1}$)
3.0	0.86543
6.0	0.80176
9.0	0.77434
12.3	0.69852

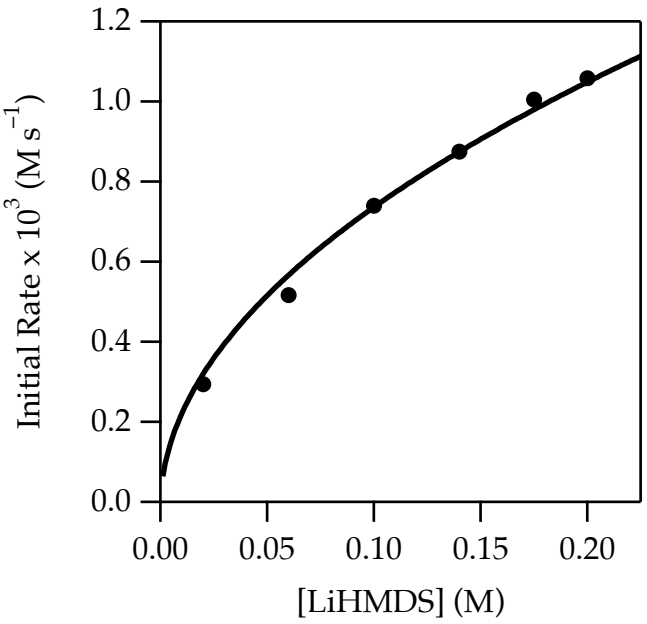


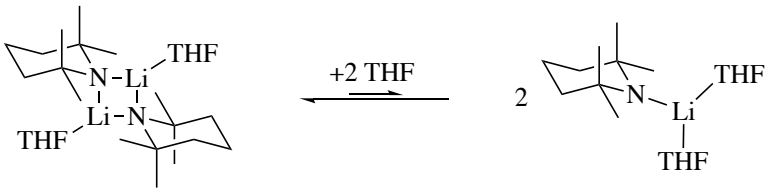
Figure A.2.13. Plot of k_{obsd} vs. LiTMP concentration in 6.0 M THF with hexane cosolvent for the metalation of **4** (0.010 M) at –40 °C measured with IR spectroscopy (1655 cm^{-1}). The curve depicts the result of an unweighted least-squares fit to $y = ax^n$ ($a = 2.7 \pm 0.1$, $n = 0.57 \pm 0.02$).

[THF] (M)	Initial Rate × 10^3 ($M\ s^{-1}$)
0.025	0.29389
0.070	0.74015
0.11	0.87481
0.16	1.0051
0.20	1.058
0.25	0.51666

III. Derivations

D-A.2.1. LiTMP-meidated enolization: THF

To simplify the discussion of the mechanistic model, we introduce the following shorthand: A = a LiTMP subunit, and S = THF. As shown below, A_2S_2 corresponds to the disolvated LiTMP dimer, and AS_2 corresponds to disolvated LiTMP monomer.



A_2S_2 **AS_2**

Given $K_{eq} = [AS_2]^2/\{[A_2S_2][S]^2\}$, and $2[A_2S_2] + [AS_2] = [A_{total}]$, one can solve for $[A_2S_2]$ as a function of $[A_{total}]$ and [S]:

$$K_{eq} = \frac{\left[AS_2\right]^2}{\left[A_2S_2\right]\left[S\right]^2} = \frac{\left(\left[A_{total}\right] - 2\left[A_2S_2\right]\right)^2}{\left[A_2S_2\right]\left[S\right]^2}$$

Rearranging,

$$4\left[A_2S_2\right]^2 - \left(4\left[A_{total}\right] + K_{eq}\left[S\right]^2\right)\left[A_2S_2\right] + \left[A_{total}\right]^2 = 0$$

Applying the quadratic equation to $[A_2S_2]$ gives:

$$\left[A_2S_2\right] = \frac{\left(4\left[A_{total}\right] + K_{eq}\left[S\right]^2\right) - \sqrt{\left(4\left[A_{total}\right] + K_{eq}\left[S\right]^2\right)^2 - 16\left[A_{total}\right]}}{8} = \frac{4\left[A_{total}\right] + K_{eq}\left[S\right]^2 - \sqrt{K_{eq}}\left[S\right]\sqrt{K_{eq}\left[S\right]^2 + 8\left[A_{total}\right]}}{8}$$

D-A.2.2. Mathematica simulation of LiTMP order vs. percent monomer

Knowing that LiTMP exists as a dimer-monomer equilibrium we sought to develop a simulation that illustrated how the order in LiTMP (base order) varied with percent monomer relative to the total base titer. Consider the following equation:

$$1/2\ A_2 + 2S \underset{}{\overset{K_{eq}}{\rightleftharpoons}} AS_2 \xrightarrow{k} [AS_2]^{\ddagger}$$

for which $K_{eq} = [A]^2/\{[A_2][S]^2\}$. For simplicity, the model assumes reactivity funnels exclusively through a monomer-based transition state. Within this section, text within boxes contains executable code that can be directly pasted into *Mathematica*, and images beneath the code are screenshots of the actual input/output. We first solve for $[A_2]$ and [A]:

```
Solve[{keq == a^2/(a2*s^2), a0 == 2*a2 + a}, {a2, a}]
```

```
Solve[{keq == a^2 / (a2 * s^2), a0 == 2 a2 + a}, {a2, a}]
{{a2 → 1/8 (4 a0 + keq s^2 - Sqrt[keq] s Sqrt[8 a0 + keq s^2]), a → 1/4 (-keq s^2 + Sqrt[keq] s Sqrt[8 a0 + keq s^2])},
 {a2 → 1/8 (4 a0 + keq s^2 + Sqrt[keq] s Sqrt[8 a0 + keq s^2]), a → 1/4 (-keq s^2 - Sqrt[keq] s Sqrt[8 a0 + keq s^2])}}
```

We chose the first set of roots, which correspond to the realistic case of all concentrations being positive. We then solve for the concentration of dimer (d) and monomer (m) as a function of the fraction of monomer (r) by normality:

```
Solve[{2 d + m == 0.1, m/(2 d + m) == r/100}, {d, m}]
```

```
Solve[{2 d + m == 0.1, m / (2 d + m) == r / 100}, {d, m}]
{{d → 0.05 - 0.0005 r, m → 0.001 r}}
```

We can then use the equilibrium expression to solve for the equilibrium constant (K_{eq}) as a function of r by substituting in the previous result:

```
m^2/(d*s^2) /. {d -> 0.05` - 0.0005` r, m -> 0.001` r}
```

```
m^2 / (d*s^2) /. {d → 0.05` - 0.0005` r, m → 0.001` r}
```

$$\frac{1.\times 10^{-6}\, r^2}{(0.05 - 0.0005\, r)\, s^2}$$

With this is hand, we replace all instances of the equilibrium constant (K_{eq}) in the rate expression with the solution above:

```
Simplify[k*1/4 (-keq s^2 + Sqrt[keq] s Sqrt[8 a0 + keq s^2])
/.   keq -> (1.`*^-6 r^2)/((0.05` - 0.0005` r) s^2)]
```

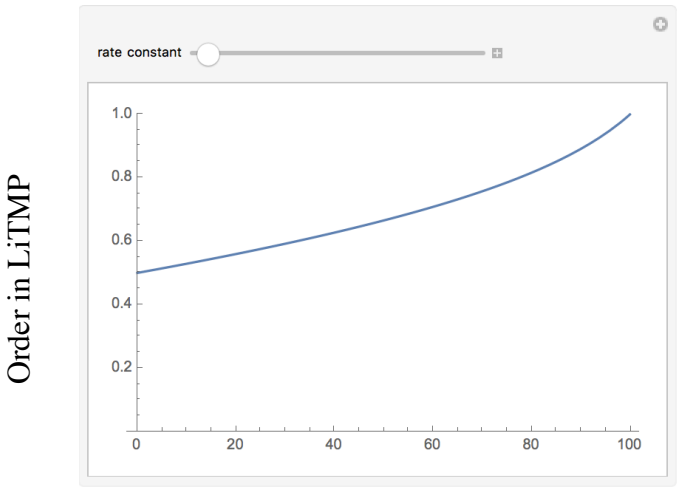
```
Simplify[k * 1/4 (-keq s^2 + Sqrt[keq] s Sqrt[8 a0 + keq s^2]) /. keq → (1.`*^-6 r^2)/((0.05` - 0.0005` r) s^2)]
```

$$k\left(-\frac{2.5`*^{-7}\, r^2}{0.05` - 0.0005` r} + 0.00025` \sqrt{8\, a0 + \frac{1.`*^{-6}\, r^2}{0.05` - 0.0005` r}}\ \sqrt{\frac{r^2}{(0.05` - 0.0005` r)}}\right)$$

The output from this substitution provides us with the necessary equation to describe LiTMP order as a function of percent monomer (observable). If one looks closely at the previous input/output, it becomes apparent that the change in solvation has no effect on the contribution of the aggregates to the total measured order—all *s* terms cancel. Therefore, only the change in aggregation state in conjunction with the shifting ground state influences the measured order.

We can now plot the LiTMP order as a function of percent monomer for 0.1 N LiTMP as follows:

```
Manipulate[Plot[n /.FindFit[Flatten[Table[{k (-((2.5`*^-7 r^2)/(0.05` -
0.0005` r)) + 0.00025` Sqrt[8 a0 + (1.`*^-6 r^2)/(0.05` - 0.0005` r)]
Sqrt[r^2/(0.05` - 0.0005` r) ] )}, {a0, 0, 0.25,0.0001}]], a*x^n, {a, n}, x],
{r, 0, 100}, PlotRange -> {0, 1}], {{k, 1, "rate constant"}, 0, 100}]
```

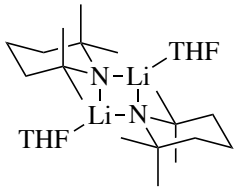


We first generate a table of data, which corresponds to rate vs. base concentration (a0) at a given percent monomer (r). We then fit to a simple power function to obtain the LiTMP order. We repeat this calculation incrementally from r=0 (no observable monomer) to r=100 (100% observable monomer). We include a provision to adjust the rate constant, *k*, but add there is no effect on the plot shape.

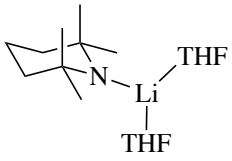
IV: Ground State Computations

Chart A.2.2.

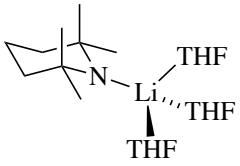
THF



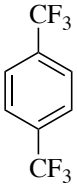
A_2S_2



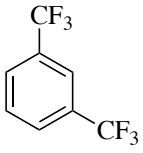
AS_2



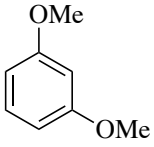
AS_3



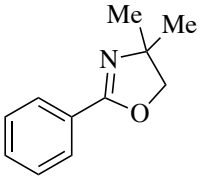
1



2

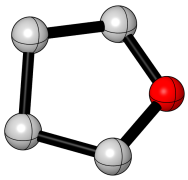


3



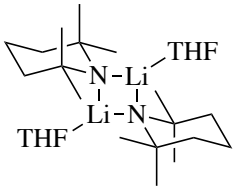
4

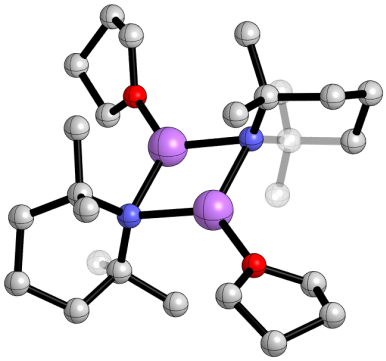
Table A.2.2. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant ground states of LiTMP/THF-mediated ortholithiations with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures at the given temperature.)



THF (–78 °C)
G = –232.357946
G_{MP2} = –145317.665

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
H	0.36944100	0.05245400	1.03607400
H	0.78366900	0.39304900	-0.65835500
C	-0.43145400	-1.42747100	-0.35907500
H	-0.36819400	-1.58569300	-1.44243900
H	0.17898100	-2.19202000	0.13156300
C	-1.89873200	-1.42780000	0.09478400
H	-2.50889400	-2.19240900	-0.39610500
H	-1.96191900	-1.58645800	1.17808700
C	-2.33082600	-0.00036200	-0.26378100
H	-2.70107000	0.05220800	-1.29954200
H	-3.11413200	0.39228800	0.39526100
O	-1.16547600	0.82075200	-0.13234900

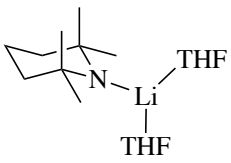


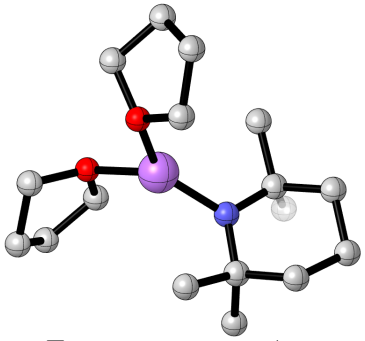


A_2S_2 (–78 °C)
G = –1296.456254
G_{MP2} = –810668.178

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
H	-0.93184200	-0.53199300	0.23483900
H	0.76398100	-0.77620000	-0.14547200
C	0.39424400	0.92553200	1.14842500
H	0.49607000	0.36089700	2.08628100
H	1.38887300	1.34097900	0.92492200
C	-0.59074100	2.11271100	1.35418200
N	-0.91199800	2.83953700	0.09804500
C	-1.19052500	1.98766800	-1.08691600
C	-0.16564200	0.83494700	-1.26810400
H	-0.45998600	0.20130700	-2.11701800
H	0.81030200	1.27422700	-1.52577600
C	-1.08637200	2.87248700	-2.34340400
H	-1.79871500	3.70871300	-2.31125000
H	-1.30222600	2.30033800	-3.25475200
H	-0.07780800	3.29034000	-2.44162400
C	-2.62305200	1.36871800	-1.12858100
H	-2.79315800	0.63944800	-0.33295700

H	-3.37448500	2.15846400	-1.02721200	H	-2.14117100	7.87703700	-2.84736700
H	-2.80163800	0.85238300	-2.08231700	H	-2.63602900	6.26131600	-2.31489200
Li	-2.25521100	4.44387100	0.05504500	H	0.52788500	8.36079900	-0.30704200
N	-1.19582100	6.20192000	0.06674400	H	-0.32722200	9.08572700	-1.65578600
Li	0.12525800	4.60742000	0.03482700	C	-2.51416500	6.06962900	2.16250100
O	2.14443600	4.71693200	-0.01996500	H	-2.70071200	6.51421800	3.14897600
C	2.97341700	5.69906500	0.64722800	H	-3.47395000	5.99497500	1.63874700
H	2.96245800	5.48369100	1.72274300	H	-2.14234600	5.05280800	2.34241100
H	2.53422300	6.68673900	0.48466300	C	-0.25234100	7.11367500	2.22986300
C	4.37364000	5.53987700	0.04790300	H	-0.49842100	7.58407100	3.19331600
H	4.48536500	6.17263000	-0.84048100	H	0.49303800	7.74281700	1.73434500
H	5.16138300	5.81013700	0.75725600	H	0.22031400	6.14783200	2.44367100
C	4.39211600	4.05525800	-0.34844200	O	-4.27873200	4.23550500	-0.07206100
H	5.13367500	3.82062000	-1.11779600	C	-5.07033400	3.48555900	0.88149200
H	4.59556500	3.42668700	0.52654300	H	-5.05101100	4.01470100	1.84329900
C	2.95899300	3.84315600	-0.83461300	H	-4.60715000	2.50477100	1.00733000
H	2.84399100	4.13309200	-1.88793300	C	-6.48110600	3.43531000	0.29520700
H	2.58703200	2.82411300	-0.70653300	H	-6.57563300	2.59519300	-0.40277000
C	-1.51248300	6.91137100	1.33743700	H	-7.24839400	3.32535800	1.06727300
C	-2.19060500	8.28866000	1.12592900	C	-6.56056000	4.77152500	-0.45832500
H	-2.39609300	8.74930200	2.10188500	H	-7.32228100	4.78344600	-1.24346600
H	-3.17014000	8.11030700	0.66525000	H	-6.77610600	5.59046100	0.23810900
C	-1.37269200	9.25280300	0.24696800	C	-5.14427300	4.90660200	-1.02073300
H	-0.75413400	9.90898000	0.87221100	H	-5.04615000	4.40613300	-1.99267800
H	-2.05791500	9.91730600	-0.29441300	H	-4.80406300	5.93919200	-1.11987800
C	-0.47097800	8.49160900	-0.74285800	C	0.12507800	3.08648500	2.31574000
C	-1.00294300	7.08496600	-1.11492600	H	-0.50846500	3.94147300	2.57203800
C	0.04511900	6.46065700	-2.06170100	H	0.38902100	2.58793400	3.25712600
H	1.02262300	6.38951900	-1.57161700	H	1.05517200	3.46312700	1.87324500
H	0.16783400	7.06012200	-2.97358200	C	-1.83783500	1.59687500	2.13255700
H	-0.25566900	5.45642400	-2.37671800	H	-1.55797100	1.19091500	3.11479700
C	-2.30066600	7.24477900	-1.96151400	H	-2.53868200	2.42308100	2.30241500
H	-3.11595500	7.68660200	-1.38074200	H	-2.37512700	0.80835700	1.59934000

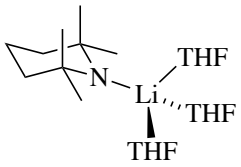


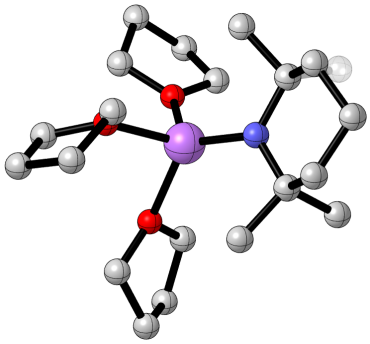


AS_2 (–78 °C)
G = –880.575136
G_{MP2} = –550642.897

Atom	X	Y	Z	Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000	H	0.75391800	-0.74172200	-0.29845100

H	0.56133000	0.88448500	0.33118600
C	-0.89292400	0.35723200	-1.19268800
H	-0.29118200	0.78020100	-2.01091300
H	-1.34502100	-0.57012800	-1.57584200
C	-2.04274800	1.32709400	-0.79672700
N	-2.77693400	0.86481800	0.38098700
C	-2.00128400	0.42878100	1.54168400
C	-0.85389600	-0.54473100	1.15022800
H	-0.22342800	-0.77560400	2.02190500
H	-1.30823300	-1.49291600	0.82429600
C	-1.41100100	1.58316700	2.41116100
H	-2.19795300	2.30976900	2.64572100
H	-1.00083700	1.20555400	3.35896600
H	-0.60619700	2.12364800	1.90638000
C	-2.96902700	-0.33856100	2.46966100
H	-3.79424100	0.31442400	2.79169700
H	-2.47000700	-0.70442100	3.37624200
H	-3.39550700	-1.20455800	1.94623000
Li	-4.62479000	0.59603900	0.31422200
C	-1.46847600	2.77415100	-0.68467700
H	-2.25527000	3.45606400	-0.34049600
H	-0.63992300	2.84571700	0.02462300
H	-1.09693700	3.13798000	-1.65356400
C	-3.04656700	1.36567000	-1.97021400
H	-3.87216700	2.05878000	-1.74701100
H	-3.47130100	0.36959300	-2.15077800
H	-2.57892100	1.70606500	-2.90303400
C	-7.09920100	2.31019900	0.00498000
H	-8.03925300	2.33551800	0.57610300
H	-7.18987700	1.56883800	-0.79333000
C	-6.69360500	3.70457300	-0.46459500
H	-5.95408500	3.62509200	-1.26912300
H	-7.54058300	4.29230100	-0.83154600
C	-6.05377200	4.29445700	0.80676700
H	-5.29068400	5.04454400	0.58120500
H	-6.81689800	4.77261800	1.43066900
C	-5.45828800	3.06384300	1.52118300
H	-4.37361100	2.97283700	1.41490800
H	-5.72523400	3.02820000	2.58331000
O	-6.02206400	1.89162800	0.86177300
C	-6.76867200	-1.52092800	0.53848900
H	-7.65807700	-1.66175100	-0.09358400
H	-7.00230700	-0.79778500	1.32375200
C	-6.22446400	-2.85541500	1.04057800
H	-5.55814500	-2.68799400	1.89365800
H	-7.01453300	-3.54623700	1.35014300
C	-5.43131400	-3.35502500	-0.18213100
H	-4.59847200	-4.00704100	0.09542700
H	-6.08546800	-3.91939000	-0.85573300
C	-4.94725800	-2.05587900	-0.85914600
H	-3.89089900	-1.83517200	-0.68368300
H	-5.13904400	-2.05178300	-1.93783200
O	-5.69768200	-0.96863900	-0.24894500

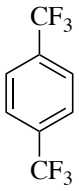


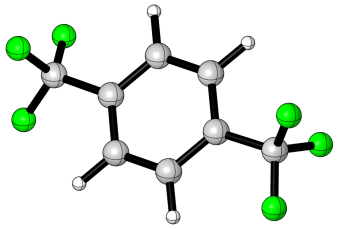


AS_3 (–78 °C)
G = –1112.914623
G_{MP2} = –695956.399

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
H	-0.93184200	-0.53199300	0.23483900
H	0.76398100	-0.77620000	-0.14547200
C	0.39424400	0.92553200	1.14842500
H	0.49607000	0.36089700	2.08628100
H	1.38887300	1.34097900	0.92492200
C	-0.59074100	2.11271100	1.35418200
N	-0.91199800	2.83953700	0.09804500
C	-1.19052500	1.98766800	-1.08691600
C	-0.16564200	0.83494700	-1.26810400
H	-0.45998600	0.20130700	-2.11701800
H	0.81030200	1.27422700	-1.52577600

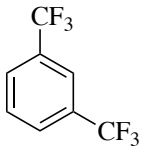
C	-1.08637200	2.87248700	-2.34340400
H	-1.79871500	3.70871300	-2.31125000
H	-1.30222600	2.30033800	-3.25475200
H	-0.07780800	3.29034000	-2.44162400
C	-2.62305200	1.36871800	-1.12858100
H	-2.79315800	0.63944800	-0.33295700
H	-3.37448500	2.15846400	-1.02721200
H	-2.80163800	0.85238300	-2.08231700
Li	-2.25521100	4.44387100	0.05504500
N	-1.19582100	6.20192000	0.06674400
Li	0.12525800	4.60742000	0.03482700
O	2.14443600	4.71693200	-0.01996500
C	2.97341700	5.69906500	0.64722800
H	2.96245800	5.48369100	1.72274300
H	2.53422300	6.68673900	0.48466300
C	4.37364000	5.53987700	0.04790300
H	4.48536500	6.17263000	-0.84048100
H	5.16138300	5.81013700	0.75725600
C	4.39211600	4.05525800	-0.34844200
H	5.13367500	3.82062000	-1.11779600
H	4.59556500	3.42668700	0.52654300
C	2.95899300	3.84315600	-0.83461300
H	2.84399100	4.13309200	-1.88793300
H	2.58703200	2.82411300	-0.70653300
C	-1.51248300	6.91137100	1.33743700
C	-2.19060500	8.28866000	1.12592900
H	-2.39609300	8.74930200	2.10188500
H	-3.17014000	8.11030700	0.66525000
C	-1.37269200	9.25280300	0.24696800
H	-0.75413400	9.90898000	0.87221100
H	-2.05791500	9.91730600	-0.29441300
C	-0.47097800	8.49160900	-0.74285800
C	-1.00294300	7.08496600	-1.11492600
C	0.04511900	6.46065700	-2.06170100
H	1.02262300	6.38951900	-1.57161700
H	0.16783400	7.06012200	-2.97358200
H	-0.25566900	5.45642400	-2.37671800
C	-2.30066600	7.24477900	-1.96151400
H	-3.11595500	7.68660200	-1.38074200
H	-2.14117100	7.87703700	-2.84736700
H	-2.63602900	6.26131600	-2.31489200
H	0.52788500	8.36079900	-0.30704200
H	-0.32722200	9.08572700	-1.65578600
C	-2.51416500	6.06962900	2.16250100
H	-2.70071200	6.51421800	3.14897600
H	-3.47395000	5.99497500	1.63874700
H	-2.14234600	5.05280800	2.34241100
C	-0.25234100	7.11367500	2.22986300
H	-0.49842100	7.58407100	3.19331600
H	0.49303800	7.74281700	1.73434500
H	0.22031400	6.14783200	2.44367100
O	-4.27873200	4.23550500	-0.07206100
C	-5.07033400	3.48555900	0.88149200
H	-5.05101100	4.01470100	1.84329900
H	-4.60715000	2.50477100	1.00733000
C	-6.48110600	3.43531000	0.29520700
H	-6.57563300	2.59519300	-0.40277000
H	-7.24839400	3.32535800	1.06727300
C	-6.56056000	4.77152500	-0.45832500
H	-7.32228100	4.78344600	-1.24346600
H	-6.77610600	5.59046100	0.23810900
C	-5.14427300	4.90660200	-1.02073300
H	-5.04615000	4.40613300	-1.99267800
H	-4.80406300	5.93919200	-1.11987800
C	0.12507800	3.08648500	2.31574000
H	-0.50846500	3.94147300	2.57203800
H	0.38902100	2.58793400	3.25712600
H	1.05517200	3.46312700	1.87324500
C	-1.83783500	1.59687500	2.13255700
H	-1.55797100	1.19091500	3.11479700
H	-2.53868200	2.42308100	2.30241500
H	-2.37512700	0.80835700	1.59934000

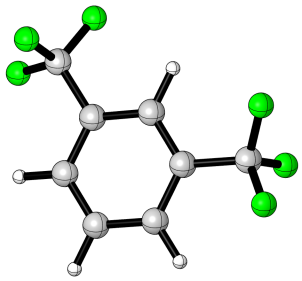




1 (–78 °C)
G = –906.234214
G_{MP2} = –567194.695

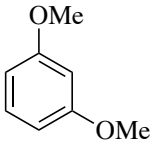
Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	-1.50628400	0.01470000	-0.04260800
C	-2.20922400	-1.19482000	-0.03627300
H	-1.66871600	-2.13528900	-0.05072600
C	-3.59950900	-1.18619100	-0.02081600
H	-4.15079200	-2.12131700	-0.01888900
C	-4.28918300	0.03108900	-0.01172600
C	-3.58864500	1.23692100	-0.02045500
H	-4.12890600	2.17661700	-0.01802000
C	-2.19431200	1.22845000	-0.03538000
H	-1.64406900	2.16292800	-0.04841500
C	-5.79572400	0.00760500	0.00414100
F	-6.32789500	1.24690200	0.01107900
F	-6.28810300	-0.64012600	-1.07605900
F	-6.26445900	-0.64218400	1.09352400
F	0.52971200	1.12319100	-0.53001300
F	0.50791700	-1.05178200	-0.67883200
F	0.45657300	-0.09336900	1.26974700

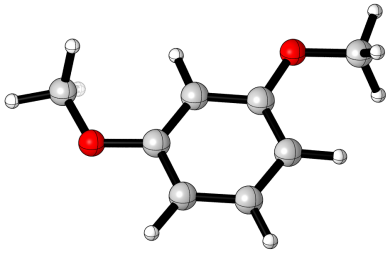




2 (–78 °C)
G = –906.235281
G_{MP2} = –567195.185

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	1.30595600	0.75079400	0.02869900
C	2.51087200	0.04811000	-0.00223900
H	2.51087200	-1.03580500	-0.00223900
C	3.71578800	0.75079400	-0.03317700
C	3.71864200	2.14811600	-0.03447700
C	2.51087200	2.84347200	-0.00223900
H	2.51087200	3.92917900	-0.00223900
C	1.30310200	2.14811600	0.02999900
H	0.36063200	2.68457300	0.06144400
H	4.66111200	2.68457300	-0.06592200
C	5.02174400	0.00000000	-0.00447800
F	5.99786900	0.67456800	-0.65066100
F	4.91477200	-1.21641600	-0.58010000
F	5.45208700	-0.19861100	1.26252300
F	-0.97612500	0.67456800	0.64618300
F	0.10697200	-1.21641600	0.57562100
F	-0.43034300	-0.19861100	-1.26700100

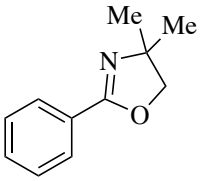


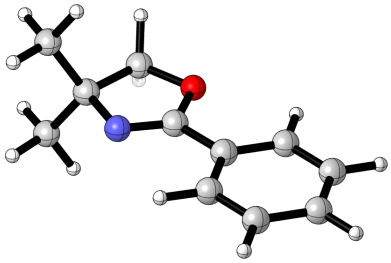


3 (–40 °C)
G = –461.153141
G_{MP2} = – 288461.342

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
O	0.34817800	1.37452300	-0.00001500
C	1.67304100	1.70514300	-0.00001000
C	2.71155100	0.77588800	-0.00001100
C	4.04380600	1.22219100	-0.00000700
C	4.33789500	2.58732100	-0.00000500
C	3.27612800	3.50243100	-0.00000500
C	1.95495600	3.08278900	-0.00000700
H	1.12937800	3.78661700	-0.00000800
H	3.49779300	4.56650100	-0.00000100

Atom	X	Y	Z
H	5.36001400	2.94621900	0.00000100
O	4.97997100	0.22564000	-0.00000800
C	6.34872200	0.59497500	-0.00000700
H	6.61076600	1.17599000	-0.89434600
H	6.91223000	-0.34027600	-0.00001200
H	6.61076400	1.17598200	0.89433800
H	2.53636000	-0.29287000	-0.00001200
H	0.37882800	-0.51267300	0.89423200
H	0.37882100	-0.51269100	-0.89422300
H	-1.09131600	-0.03310600	0.00000500





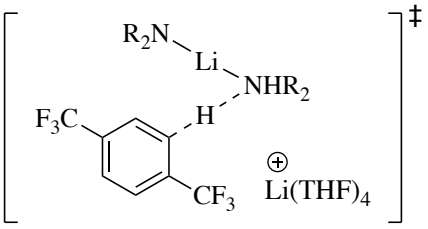
4 (–40 °C)
G = –556.788405
G_{MP2} = –348261.434

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	0.27714300	-1.53802700	0.00004300
N	-1.07582200	-2.13027000	0.00005300
C	-1.91843800	-1.17072800	0.00003200
C	-3.38476300	-1.30798200	0.00003500
C	-3.95446200	-2.59038700	0.00002800
C	-5.33809000	-2.73875000	0.00003300
C	-6.16538700	-1.61134200	0.00004500
C	-5.60181600	-0.33425100	0.00005100
C	-4.21589600	-0.17930500	0.00004600
H	-3.77170300	0.81013500	0.00004900
H	-6.24192800	0.54387100	0.00006100
H	-7.24582300	-1.72923000	0.00004900

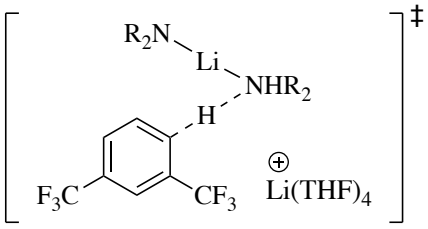
Atom	X	Y	Z
H	-5.77388500	-3.73418800	0.00002700
H	-3.29600600	-3.45277000	0.00002100
O	-1.43895000	0.11276300	0.00000300
C	1.02639500	-1.98728300	-1.26304900
H	2.03452800	-1.55554300	-1.29352100
H	1.11620500	-3.07792800	-1.28304900
H	0.48890800	-1.67411400	-2.16469100
C	1.02638000	-1.98721400	1.26317000
H	1.11618400	-3.07785800	1.28323400
H	2.03451400	-1.55547700	1.29362700
H	0.48888400	-1.67399000	2.16478800
H	0.38213400	0.50885700	-0.89132700
H	0.38214200	0.50890800	0.89129500

V. Transition State Computations

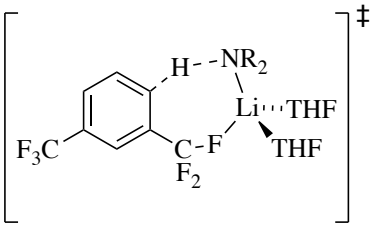
Chart A.2.3.



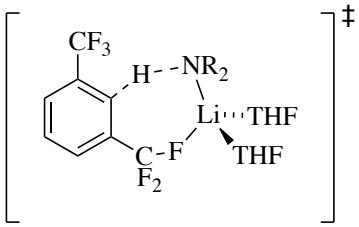
1-A_2S_4



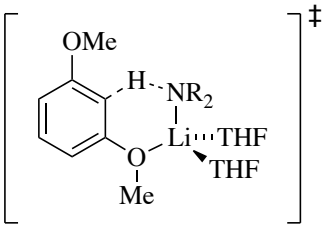
2-A_2S_4



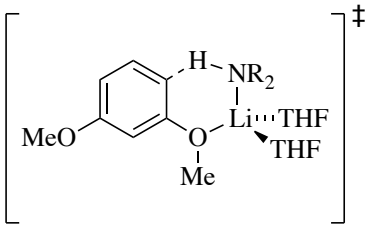
2-AS_2 (external)



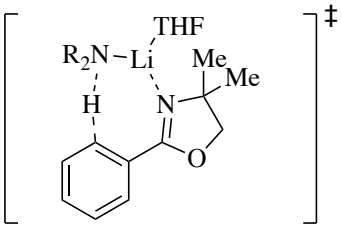
2-AS_2 (internal)



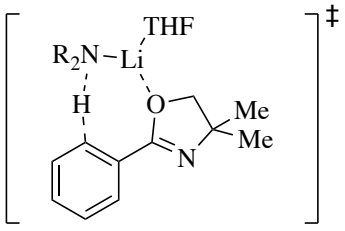
3-AS_2 (internal)



3-AS_2 (external)

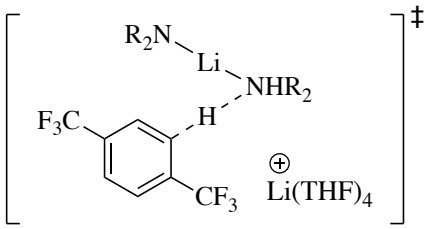


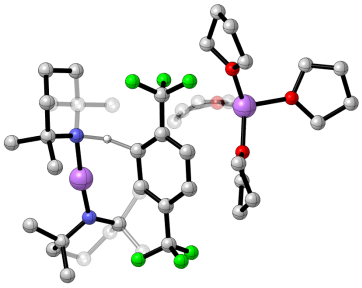
4-AS (N-bound)



4-AS(O-bound)

Table A.2.3. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant transition states of LiTMP/THF-mediated ortholithiation of **1** at –78 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)



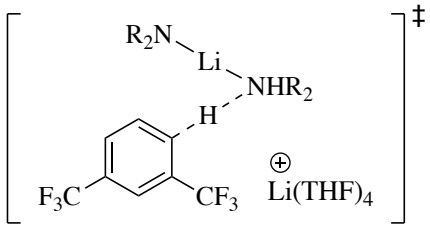


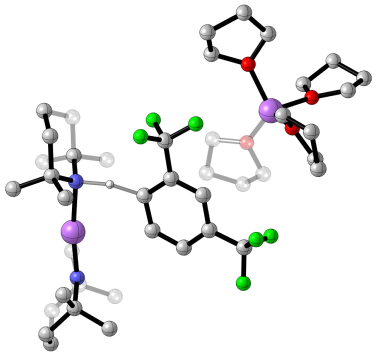
1-A_2S_4
G = –2667.335463
G_{MP2} = –1668467.937

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	0.71694400	-1.14002400	-0.66933800
C	0.35965800	-1.44299000	-1.99328600
C	0.97976800	-2.49963900	-2.65080800
H	0.73063700	-2.73313800	-3.68102200
C	1.94507800	-3.24462900	-1.96537300
C	2.29549800	-2.90837600	-0.65300800
C	1.71231500	-1.83506600	0.04916800
H	3.07397000	-3.49913400	-0.16951800
C	2.57111100	-4.43194100	-2.63982500
F	1.84437300	-5.57196900	-2.41989900
F	3.81745700	-4.68722200	-2.20167900
F	2.63394200	-4.28645800	-3.98508800
H	-0.38831900	-0.85195000	-2.51270000
F	-1.04838700	0.47886100	-0.73456600
F	-0.55140900	-0.37012800	1.19845500
F	0.78962000	1.06218300	0.26431700
H	2.41346100	-1.54184300	1.25741800
Li	3.84453600	-3.41564000	2.25821200
N	3.29682200	-1.45086300	2.30397300
C	2.53241700	-1.10962600	3.53739700
C	2.05527500	0.36892400	3.54739100
C	3.17503100	1.36307600	3.22249700
H	2.76281300	2.37860900	3.14537800
H	3.90565000	1.39575300	4.04165600
C	3.86151000	0.97202800	1.90994700
C	4.37866600	-0.49034600	1.92207300
C	5.64472600	-0.56949200	2.81879600
H	5.96215500	-1.60712600	2.95776100
H	6.47384200	-0.02633900	2.34612900
H	5.50329100	-0.13077900	3.80876300
C	4.84404900	-0.84426200	0.49429100
H	5.21634200	-1.87571700	0.44083900
H	5.66237100	-0.18248200	0.18565400
H	4.03575400	-0.74207500	-0.23325800
H	4.69301800	1.65846600	1.69480800
H	3.13988400	1.07754000	1.09069800
H	1.60587400	0.60515500	4.52368100
H	1.26274700	0.48306200	2.79903600
C	3.29773900	-1.41334300	4.85526500
H	2.60940300	-1.37745500	5.71150000
H	4.10312600	-0.70608300	5.06229800
H	3.73722700	-2.41813300	4.82048000
C	1.28017800	-2.01071200	3.56208400
H	1.56137200	-3.06480500	3.66972700
H	0.69724100	-1.90211400	2.64500800
H	0.64242100	-1.74724400	4.41740000
N	4.21621200	-5.25737600	2.14349300
C	3.24032200	-6.34485000	2.14894600
C	3.54359800	-7.40944700	3.24400600
C	4.99310600	-7.89970600	3.19338700
H	5.19235000	-8.58724200	4.02778400
H	5.16592300	-8.47994500	2.27642700
C	5.94665000	-6.70262800	3.25066500
C	5.63238700	-5.64254700	2.15710000
C	6.18674000	-6.14238800	0.78626600
H	5.86260700	-5.46355600	-0.01009700
H	7.28572400	-6.17763900	0.78765700
H	5.83704900	-7.14540300	0.52745400
C	6.44771600	-4.38000900	2.50045200

H	6.32862300	-3.61506700	1.72030900
H	7.52128400	-4.59531500	2.57685200
H	6.11870300	-3.95924600	3.45974800
H	6.99101600	-7.04014400	3.17127500
H	5.83938900	-6.22005500	4.23343400
H	2.84723300	-8.25893600	3.16121800
H	3.36959500	-6.94513800	4.22629900
C	3.05178400	-7.07394900	0.78019200
H	2.92084900	-6.34182400	-0.02270000
H	3.90824700	-7.69782600	0.51330600
H	2.17147900	-7.73575100	0.79635000
C	1.86952100	-5.72603000	2.48886800
H	1.59186900	-4.96787300	1.74338800
H	1.91014200	-5.24482000	3.47345100
H	1.07793800	-6.49084400	2.51184400
C	-5.57785700	-5.70085500	0.58925800
H	-5.34665100	-6.69800000	0.97815500
H	-4.97842500	-5.52870900	-0.31005400
C	-7.08118700	-5.48968000	0.34961000
H	-7.66903600	-6.18135400	0.96303000
H	-7.35881600	-5.65113200	-0.69559600
C	-7.30585300	-4.04230400	0.81812900
H	-7.02789700	-3.33161500	0.03100200
H	-8.33984800	-3.84075000	1.11203800
C	-6.33044900	-3.94268500	1.98744300
H	-5.98164300	-2.93078900	2.20520000
H	-6.75405000	-4.38128900	2.90189200
O	-5.17999300	-4.71197600	1.57536800
Li	-3.31634000	-4.08714100	1.85427500
O	-2.22208200	-4.97016100	0.51356200
C	-1.78203100	-6.35297700	0.61466500
H	-2.68066200	-6.97992400	0.66267000
H	-1.21467300	-6.47695700	1.54178000
C	-0.93936100	-6.63137500	-0.63884400
H	-1.10137500	-7.64150200	-1.02562900
H	0.12693200	-6.52189400	-0.42130800
C	-1.38799200	-5.53177700	-1.61479400
H	-0.62776600	-5.31081700	-2.36523200
H	-2.32000400	-5.80909300	-2.12300000
C	-1.62649700	-4.36327000	-0.66733800
H	-0.69066200	-3.86844500	-0.38794100
H	-2.33169900	-3.61447900	-1.03765000
O	-3.41416600	-2.12183600	1.86439100
C	-3.72650000	-1.24286000	0.74971200
H	-4.66656000	-1.59985600	0.31362500
H	-2.93362500	-1.31324000	0.00085800
C	-3.83968800	0.17870400	1.33119500
H	-4.69392300	0.72445800	0.92065600
H	-2.93317700	0.74231900	1.10135700
C	-3.95539000	-0.05945000	2.84754800
H	-3.58293900	0.78196100	3.43859200
H	-4.99560100	-0.24951300	3.13910100
C	-3.11541000	-1.31811300	3.03321800
H	-2.04461800	-1.08961100	3.05299800
H	-3.37663900	-1.91821300	3.90801600
O	-2.74414200	-4.67316300	3.63630200
C	-1.36980500	-4.46456800	4.07961400
H	-1.30501800	-3.47299300	4.54066000
H	-0.72147100	-4.48709500	3.20143800
C	-1.09277500	-5.57962700	5.08501700
H	-0.33339800	-5.29332600	5.81722200
H	-0.74065800	-6.48107800	4.57169100
C	-2.48054000	-5.81019100	5.70302000
H	-2.59016800	-6.79363300	6.16903900
H	-2.69424100	-5.04846700	6.46189800
C	-3.40336100	-5.63458400	4.49583300
H	-3.52637000	-6.57528400	3.94350500
H	-4.39415500	-5.24581800	4.74977900

Table A.2.4. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant transition states of LiTMP/THF-mediated ortholithiation of **2** at –78 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

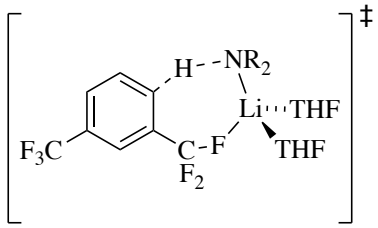


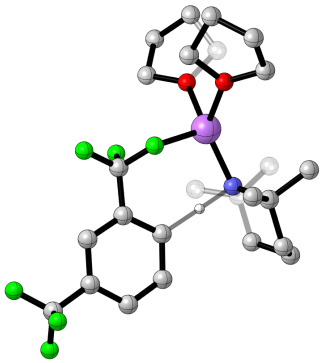


2-A_2S_4
G = –2667.337914
G_{MP2} = –1668467.049

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	0.69713800	-1.30409400	0.25979700
C	0.04105700	-2.48219600	-0.11146300
C	0.66289100	-3.71149700	0.11412900
C	1.92769800	-3.74225400	0.71168100
C	2.55974900	-2.54531300	1.05485900
C	1.98468300	-1.27582900	0.83788600
H	3.55427700	-2.61857400	1.50207700
H	2.42024600	-4.69444800	0.88948000
C	-0.05901200	-4.97074600	-0.23677500
F	-0.74611300	-4.86637100	-1.40720000
F	-1.01021900	-5.30709900	0.70269900
F	0.74995200	-6.03854200	-0.34097600
H	-0.93918200	-2.45262500	-0.57579200
F	0.50948900	0.70112200	-1.03440300
F	-1.34016300	-0.15260400	-0.27817100
F	0.03750000	0.83242300	1.08207400
H	2.84316600	-0.18566100	1.12825200
C	-5.06674200	-1.64193700	4.78678200
H	-4.59557400	-0.65615000	4.75204600
H	-4.43789200	-2.31459600	5.38247200
C	-6.51082900	-1.62227100	5.28807200
H	-7.00631700	-0.68923600	4.99511400
H	-6.57579200	-1.71389700	6.37584900
C	-7.12496600	-2.81465400	4.53872000
H	-6.86318600	-3.75495800	5.03715200
H	-8.21457800	-2.76404600	4.46002200
C	-6.43695600	-2.72309600	3.17507400
H	-6.29816100	-3.69278900	2.68886500
H	-6.98345000	-2.06200800	2.48964700
O	-5.13304600	-2.15114200	3.43040700
Li	-3.67736200	-1.56436200	2.18042000
O	-2.09765900	-2.08184200	3.19050200
C	-1.03989200	-1.24389200	3.74290800
H	-1.48599500	-0.60926300	4.51954000
H	-0.64429300	-0.61467000	2.94486400
C	-0.00043500	-2.20785900	4.31609400
H	0.53493700	-1.77697900	5.16621400
H	0.73565800	-2.46780400	3.54909000
C	-0.85170200	-3.43130100	4.68807500
H	-0.26887800	-4.35380300	4.75965700
H	-1.36395100	-3.27376300	5.64534800
C	-1.85676700	-3.47212700	3.54005300
H	-1.44727000	-3.98847600	2.66680700
H	-2.82133700	-3.91627800	3.80618100
O	-4.10461600	-2.43129800	0.45439600
C	-4.12439600	-3.87295000	0.24599000
H	-5.02835800	-4.26793400	0.72535900
H	-3.24361700	-4.30880900	0.72141700
C	-4.14006000	-4.08336700	-1.27126900
H	-4.70139200	-4.97822300	-1.55486000
H	-3.11853700	-4.19448500	-1.64600800
C	-4.77595800	-2.78349800	-1.78720500
H	-4.52217100	-2.56480700	-2.82830900
H	-5.86847200	-2.82483800	-1.70208900
C	-4.20341300	-1.74858000	-0.82295000
H	-3.20633700	-1.41353500	-1.12569000
H	-4.84187200	-0.87177800	-0.68323000

C	-3.12889900	1.52106100	2.04457900
H	-2.11112600	1.14744700	1.95767000
H	-3.23219900	2.09912700	2.97428900
C	-3.60688100	2.30932100	0.82786400
H	-3.16402900	1.87876900	-0.07477400
H	-3.32122100	3.36352000	0.87675300
C	-5.14150300	2.09980700	0.85318800
H	-5.66144600	2.97812600	1.24695500
H	-5.53814400	1.90757600	-0.14773800
C	-5.34016400	0.88663200	1.79434900
H	-5.83430700	1.18142300	2.72996900
H	-5.90592400	0.06576900	1.34655900
O	-4.02226900	0.38527100	2.09645500
C	3.21145200	3.53971600	1.20024700
H	2.52167700	4.36746100	0.98304500
H	4.16289500	4.00661800	1.48800100
C	2.66477600	2.68279500	2.34401500
H	2.54894000	3.28397800	3.25781000
H	1.66363300	2.33239500	2.06397700
C	3.55578800	1.44699700	2.64608900
N	3.88191300	0.65208200	1.42690700
C	4.29164100	1.42176100	0.21489800
C	3.39466200	2.66467500	-0.04074700
H	3.81223300	3.25230100	-0.87075800
H	2.40606700	2.31627200	-0.36748200
C	5.77912700	1.86706300	0.25428400
H	6.43282000	1.01358400	0.47445100
H	6.08617800	2.27555900	-0.71814800
H	5.97815600	2.63475200	1.00593700
C	4.14523100	0.49850200	-1.01281400
H	4.76341600	-0.39928400	-0.91445400
H	4.46701700	1.02310900	-1.92126700
H	3.10885900	0.18296400	-1.15529100
Li	5.20361900	-0.87474500	1.84114800
N	6.20774600	-2.42742800	2.22986700
C	6.57112400	-2.79976300	3.60053000
C	8.10145500	-3.02306500	3.77651600
C	8.69090600	-3.94997800	2.71114600
H	9.78305400	-4.01100200	2.82162100
H	8.31637100	-4.97422600	2.84654400
C	8.32356100	-3.43069200	1.31921400
C	6.79077500	-3.23233500	1.15041400
C	6.12788600	-4.63138300	0.93566400
H	5.03855500	-4.52162400	0.88904200
H	6.46443900	-5.09263500	-0.00410600
H	6.35503900	-5.33826300	1.73786400
C	6.57081900	-2.46689100	-0.16911100
H	5.49849000	-2.37170000	-0.38513200
H	7.02973300	-2.98403400	-1.02217300
H	7.00815900	-1.46195900	-0.10885300
H	8.71205900	-4.10513300	0.54099100
H	8.81071500	-2.45549500	1.17138300
H	8.31964900	-3.40632300	4.78502000
H	8.59746400	-2.04485400	3.69300900
C	5.80622300	-4.04238800	4.15773300
H	4.73277200	-3.92363400	3.96793300
H	6.12169700	-4.97926500	3.69099200
H	5.95524000	-4.15604200	5.24182500
C	6.18674100	-1.62621800	4.52221300
H	5.10477800	-1.44150700	4.48709800
H	6.70604200	-0.71178300	4.21067400
H	6.44999900	-1.82603300	5.56952100
C	4.80812900	1.92616300	3.43030700
H	4.51718100	2.32585600	4.41175900
H	5.35899400	2.71507100	2.91269900
H	5.50280300	1.09802400	3.60420200
C	2.76262400	0.52583500	3.59751400
H	3.33968500	-0.36849800	3.86029100
H	1.83048000	0.19574500	3.13110200
H	2.51921400	1.05268100	4.52915500

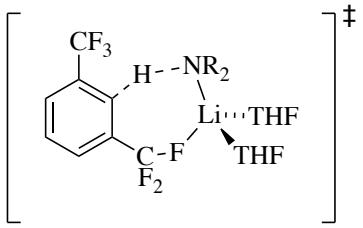


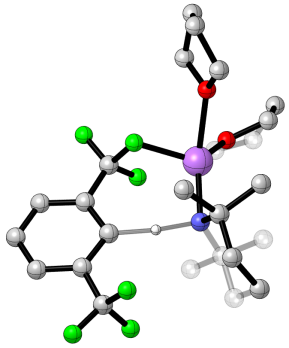


2-AS$_2$ (external)
G = –1786.784042
G_{MP2} = –1117830.948

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	1.16963400	0.91262200	0.18214000
C	0.91832800	2.29930800	0.22772900
C	2.07774300	3.09102100	0.32734200
C	3.36761600	2.56142300	0.38064900
C	3.55475100	1.17550000	0.33678100
C	2.44477900	0.33887000	0.23440600
H	2.57991400	-0.73642700	0.18926500
C	4.93066400	0.59151700	0.45744400
F	5.30691200	0.42777400	1.75168200
F	5.87025700	1.38030500	-0.11580300
F	5.02138800	-0.62845100	-0.12445200
H	4.23309300	3.21573000	0.44954000
H	1.97950100	4.17661600	0.36226400
F	0.26476600	-1.30722900	0.18788900
F	-0.57562000	0.10554400	-1.22978900
F	-1.04081500	0.29159100	0.87998800
Li	-2.56878800	1.59534500	0.37815400
N	-1.64363500	3.40296700	0.31374400
C	-1.79263200	4.21078300	-0.93471700
C	-1.38871300	3.30715700	-2.11858700
H	-0.38354400	2.89892500	-1.98724400
H	-2.09039500	2.47126100	-2.22042100
H	-1.41037000	3.87569000	-3.05669300
C	-0.85409300	5.44576500	-0.93099900
C	-0.97878700	6.28666200	0.34428700
H	-0.23908100	7.09817600	0.33431800
H	-1.96109500	6.77685300	0.38195900
C	-0.77489500	5.40721300	1.58293500
C	-1.70066400	4.16185400	1.60027600
C	-3.13410200	4.60489700	1.99878000
H	-3.85102700	3.79219000	1.83553700
H	-3.16646200	4.87904600	3.06203000
H	-3.48949600	5.47190100	1.43722500
C	-1.19826200	3.21567800	2.71321100
H	-1.83615700	2.32793800	2.79991500
H	-1.20321400	3.72895000	3.68283100
H	-0.17977500	2.87300600	2.51360000
H	-0.92921900	5.99462700	2.49921900
H	0.26715300	5.06320100	1.60538900
H	-1.05247000	6.06440200	-1.81756700
H	0.18089000	5.09012400	-1.02179100
C	-3.24743700	4.66685300	-1.21743700
H	-3.93659700	3.82103400	-1.10940400
H	-3.59349900	5.46482000	-0.55713900
H	-3.33245400	5.04049600	-2.24670900
O	-3.73448200	0.70946100	1.90014900
C	-3.70944300	-0.73829800	1.95284400
H	-2.74388200	-1.06361800	2.35714100
H	-3.80459500	-1.10609200	0.92831500
C	-4.86370100	-1.13237600	2.87178600
H	-5.80911700	-1.15621100	2.31631100
H	-4.71414300	-2.11325900	3.33238900
C	-4.86125300	0.02280300	3.88358800
H	-5.81424200	0.14707800	4.40599400
H	-4.08007300	-0.13359200	4.63629000
C	-4.52039800	1.22821300	3.00263500
H	-5.42208900	1.69912100	2.59022600
H	-3.93485000	1.99172500	3.51912600
O	-3.75026000	0.72959400	-1.06897000
C	-3.42360200	-0.13585100	-2.18939300
H	-3.04881700	-1.08318400	-1.78634000
H	-2.62804300	0.33339000	-2.77118700
C	-4.72662200	-0.31930500	-2.97445900
H	-4.81821200	0.44866300	-3.75094200
H	-4.78230200	-1.29804800	-3.45964000
C	-5.79937100	-0.11192300	-1.89419400
H	-6.77477200	0.17286100	-2.29944600
H	-5.92864600	-1.02402900	-1.29909300
C	-5.17113200	0.99296400	-1.04832400

H	-5.35998300	1.98441500	-1.48067500
H	-5.48870700	0.99543500	-0.00305700
H	-0.43271200	2.89113000	0.25613600



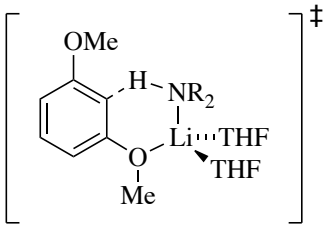


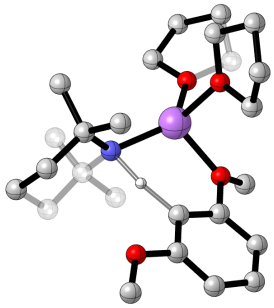
2-AS$_2$ (internal)
G = –1786.779685
G_{MP2} = –1117828.900

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	1.48855000	-0.02357800	0.11546500
C	2.15079100	1.14893800	0.54228700
C	3.55371600	0.99433400	0.61701800
C	4.22477200	-0.19256700	0.29663100
C	3.51108100	-1.31132900	-0.12422600
C	2.12761500	-1.22749600	-0.21455000
H	1.54971000	-2.08849300	-0.53544000
H	4.02684900	-2.23391700	-0.37384800
H	5.30535900	-0.24223100	0.37756000
C	4.40704300	2.15961400	1.04864600
F	4.35161800	3.19092000	0.16661700
F	4.03263400	2.65636700	2.25398000
F	5.71986000	1.83984900	1.16697400
F	-0.56774800	-1.18808600	-0.28410600
F	-0.46718800	0.87593600	-0.94762400
F	-0.61194500	0.43099000	1.16363700
Li	-1.24601700	2.38451500	0.80250800
N	0.52600400	3.41928900	0.99740100
C	0.76755100	4.46505300	-0.04925500
C	1.19009200	3.75371500	-1.35139000
H	2.12987700	3.21229600	-1.22231500
H	0.43123000	3.03453100	-1.67768000
H	1.32953900	4.48655500	-2.15596600
C	1.90109900	5.45818900	0.32430800
C	1.74218500	6.04864800	1.72551600
H	2.59506300	6.69943700	1.96036600
H	0.85017300	6.68782700	1.78097400
C	1.66036000	4.90752200	2.73965000
C	0.52957000	3.89334600	2.41793500
C	-0.82054800	4.54315500	2.84323900
H	-1.67800400	3.91892800	2.56276300
H	-0.85836100	4.67546900	3.93325700
H	-0.97686500	5.52777700	2.39567200
C	0.74150700	2.66047500	3.32302900
H	-0.03404700	1.90218700	3.16367400
H	0.71368600	2.95333800	4.38037400
H	1.70728900	2.18970700	3.12733100
H	1.51455200	5.30058800	3.75619100
H	2.61692000	4.37708900	2.73987100
H	1.94276400	6.25724000	-0.42952700
H	2.85912600	4.93167600	0.27889100
C	-0.50310300	5.29029900	-0.39517000
H	-1.32933100	4.62368700	-0.66112200
H	-0.83678100	5.92839700	0.42732700
H	-0.31122500	5.94643700	-1.25511400
O	-2.87419500	1.60839100	2.27761700
C	-3.62352400	0.46116000	1.81192600
H	-2.92271000	-0.34932200	1.58138800
H	-4.13912900	0.74595600	0.89061100
C	-4.56230700	0.08131500	2.95741000
H	-5.48259100	0.67658200	2.91781200
H	-4.84012900	-0.97664500	2.93537500
C	-3.72538800	0.46868300	4.18535200
H	-4.32220700	0.62610600	5.08863700
H	-2.98189200	-0.30780600	4.39959600
C	-3.03742800	1.74999000	3.70994600
H	-3.65634800	2.63610400	3.90427400
H	-2.05376300	1.90921800	4.15671800
O	-2.82445500	2.72323300	-0.45612200
C	-2.88923300	2.46444800	-1.88352300
H	-3.06088000	1.39142100	-2.02386700

H	-1.92658400	2.72844500	-2.32808200
C	-4.05338000	3.30878100	-2.41217900
H	-3.69735300	4.29669900	-2.72538200
H	-4.54883600	2.84065800	-3.26771000
C	-4.95884000	3.43854100	-1.17741400
H	-5.63497200	4.29728300	-1.22409300
H	-5.56387100	2.53333900	-1.04535600
C	-3.93148000	3.56517100	-0.05481900
H	-3.57431400	4.59847200	0.04532400
H	-4.27153000	3.21188400	0.92043600
H	1.39714300	2.35829100	0.81646300

Table A.2.5. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant transition states of LiTMP/THF-mediated ortholithiation of **3** at –40 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

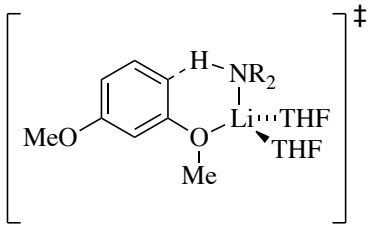


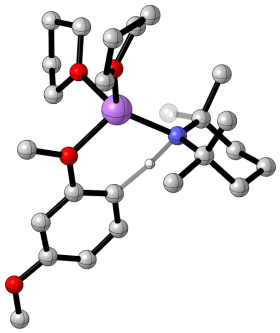


3-AS$_2$ (internal)
G = –1341.698652
G_{MP2} = –839100.800

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
H	0.33073000	-1.04645100	-0.04128400
H	0.86927900	0.65417500	-0.08991200
H	-0.68697800	0.18971400	-0.83256600
O	-0.61668600	0.31135400	1.24268700
C	-1.96867300	-0.08412300	1.41021900
C	-2.44560600	-1.24386100	0.78234000
C	-3.77675500	-1.59146000	1.00225900
C	-4.59141000	-0.81161700	1.82703800
C	-4.04571400	0.33273200	2.43066700
C	-2.71637100	0.73837800	2.24165500
O	-4.79383600	1.15220300	3.25899500
C	-6.15370800	0.83568400	3.47600600
H	-6.73019000	0.83914300	2.53992000
H	-6.27652000	-0.14360800	3.96107000
H	-6.54455700	1.61207000	4.13819100
H	-5.62468500	-1.10518500	1.97991500
H	-4.18687100	-2.48130300	0.53052200
H	-1.81684000	-1.86415800	0.15030800
Li	0.06175100	1.62370000	2.67438000
N	-1.40288100	3.03777600	3.04736200
C	-1.78770200	3.39851800	4.44268100
C	-3.19730400	4.05120000	4.51622000
C	-3.40693300	5.17477700	3.49846700
H	-4.44973600	5.51918400	3.53175000
H	-2.79350400	6.05024700	3.75296000
C	-3.06443400	4.66945100	2.09441000
C	-1.62738200	4.08972900	2.01388000
C	-0.61050800	5.26265200	2.06522600
H	0.40893400	4.88108400	2.17327400
H	-0.65924100	5.84721000	1.13626100
H	-0.79078600	5.95810000	2.88760300
C	-1.45528400	3.43665200	0.62601600
H	-0.42724800	3.07802600	0.48318300
H	-1.66258300	4.16853600	-0.16463300
H	-2.13349300	2.58998900	0.49687500
H	-3.18405100	5.47446800	1.35457600
H	-3.77305500	3.87491100	1.82400200
H	-3.38008400	4.41803400	5.53694300
H	-3.93726700	3.26695200	4.31758900
C	-0.74593400	4.30576400	5.14883200
H	0.26299600	3.89352800	5.01830900
H	-0.73589500	5.33082400	4.77128800
H	-0.95296700	4.36124300	6.22650000
C	-1.85932300	2.09641800	5.26804000
H	-0.88639600	1.59511000	5.28844200
H	-2.59589500	1.40474100	4.85255500
H	-2.14511800	2.32089200	6.30351000
O	0.74766700	0.17614000	4.04653900
C	1.61683800	0.35913500	5.18478300
H	1.22661200	1.17801100	5.80232300
H	2.60889500	0.64247200	4.81869000
C	1.60171400	-0.97106200	5.94147500
H	1.81128100	-0.84526900	7.00790600
H	2.34923700	-1.65810100	5.52658300
C	0.18235000	-1.48289000	5.65251000
H	0.07908300	-2.56512800	5.77527000
H	-0.54182500	-0.99411000	6.31374600
C	-0.03435900	-1.03971900	4.20526200
H	0.34021900	-1.78357000	3.49110800

H	-1.07175700	-0.80679300	3.95909600
O	2.01169800	1.99862000	1.97772000
C	2.98942500	0.94830900	1.83463100
H	3.02196300	0.61460200	0.78726000
H	2.66341300	0.11582200	2.46009100
C	4.31659600	1.58182700	2.24287500
H	4.40828700	1.61031700	3.33531900
H	5.18176600	1.04572800	1.84117400
C	4.16360500	3.00144000	1.67438200
H	4.79653000	3.73952400	2.17537900
H	4.41814900	3.01037800	0.60840400
C	2.66731300	3.28882000	1.87534800
H	2.47084900	3.83589000	2.80312500
H	2.22416400	3.84588100	1.04493500
H	-2.12703400	1.97342000	2.70137000



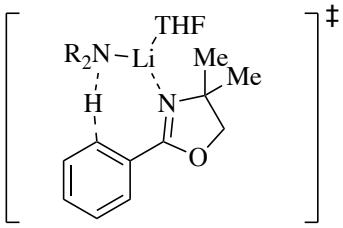


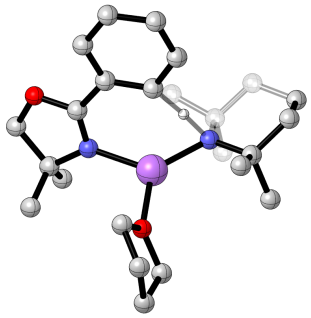
3-AS$_2$ (external)
G = –1341.69689
G_{MP2} = –839098.202

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
H	-0.63351300	-0.71210700	0.54438100
H	1.00373400	-0.41795300	-0.09956400
H	-0.42977300	0.16596100	-0.99614900
O	0.13857800	1.21788000	0.71275200
C	-1.03829400	1.91611300	1.08300100
C	-2.29290200	1.46223200	0.68268000
C	-3.42325400	2.18825000	1.09316500
C	-3.27126500	3.32805800	1.88108600
C	-1.97190400	3.72884800	2.24342600
C	-0.80752500	3.05156800	1.86902300
H	-1.88665200	4.63105800	2.85393100
H	-4.13123800	3.90310900	2.20931100
O	-4.62631900	1.67956500	0.66013000
C	-5.80260000	2.37153900	1.03031000
H	-5.80894400	3.40061100	0.64475800
H	-6.63307700	1.81676300	0.58701200
H	-5.93149100	2.40317400	2.12139100
H	-2.45562100	0.58422600	0.06676800
Li	1.81374000	1.85259600	1.72337300
N	1.80639400	3.88619300	2.19074600
C	2.07693700	4.34930800	3.57988000
C	1.57936900	5.79930700	3.82858300
C	2.04402600	6.78577700	2.75592400
H	1.60909300	7.77738500	2.94012800
H	3.13358000	6.92023700	2.80109600
C	1.62289300	6.27195000	1.37828600
C	2.13500900	4.83506700	1.08808100
C	3.64957500	4.88578700	0.75732100
H	4.03298600	3.86915100	0.62088000
H	3.82077200	5.44350200	-0.17365100
H	4.24801100	5.36709000	1.53437400
C	1.42580400	4.34743700	-0.19354700
H	1.74742500	3.33556000	-0.46720000
H	1.66478000	5.01221100	-1.03292500
H	0.34107000	4.32554200	-0.06742500
H	1.96660600	6.95418800	0.58765700
H	0.52494200	6.25965400	1.33146200
H	1.89579900	6.13327000	4.82716300
H	0.47997600	5.78667700	3.83418400
C	3.57101300	4.24067000	3.98277900
H	3.95226300	3.24058300	3.74198800
H	4.21092200	4.97009100	3.48098200
H	3.69033400	4.39545700	5.06392800
C	1.30212300	3.43051200	4.54766800
H	1.66405700	2.39939100	4.47662400
H	0.23216100	3.42876800	4.32366200
H	1.44128100	3.76718500	5.58262000
O	1.70379100	0.29760900	3.12480800
C	2.72948700	-0.28680600	3.95640300

H	3.26517100	0.52238500	4.46957400
H	3.43582100	-0.82337500	3.31500200
C	2.00656500	-1.20224100	4.95094300
H	2.53666300	-1.27845500	5.90500600
H	1.90522100	-2.21306500	4.53839300
C	0.62945800	-0.53105900	5.06730100
H	-0.15465100	-1.21046300	5.41449500
H	0.67341600	0.32121900	5.75460500
C	0.39056600	-0.04914800	3.63821900
H	-0.03083800	-0.84666000	3.01244200
H	-0.24297300	0.83591600	3.55787100
O	3.45490400	1.12998100	0.60915500
C	4.76389800	1.11030800	1.22695200
H	4.89788200	0.14499100	1.73214100
H	4.79953600	1.90996400	1.97177800
C	5.77025600	1.28823400	0.08896100
H	5.93526300	2.35257900	-0.11208500
H	6.73752000	0.82892700	0.31342200
C	5.03876600	0.62741200	-1.08883500
H	5.39724900	0.96383300	-2.06608800
H	5.14458100	-0.46306600	-1.04372300
C	3.58855000	1.03838500	-0.82947400
H	3.36202100	2.01757700	-1.26693100
H	2.85727100	0.31364000	-1.19774300
H	0.56424700	3.57328900	2.09373200

Table A.2.6. Optimized geometries at the B3LYP level of theory with 6-31G(d) basis set for relevant transition states of LiTMP/THF-mediated ortholithiation of **4** at –40 °C with free energies (Hartrees), corrected MP2 energies (kcal), and cartesian coordinates (X, Y, Z). (Note: G_{MP2} includes single-point MP2 corrections to B3LYP/6-31G(d) optimized structures.)

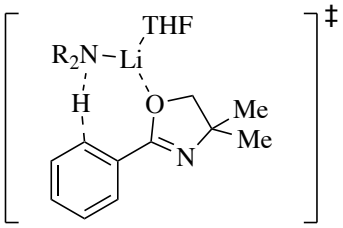


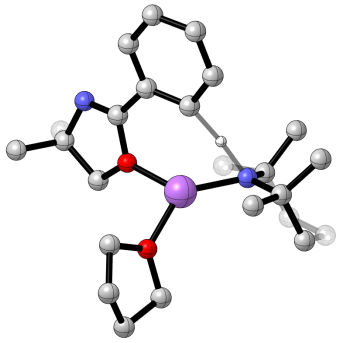


4-AS (N-bound)
G = –1204.987027
G_{MP2} = –753581.678

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	-1.28983200	0.79866200	-0.33135500
C	-2.36802300	-0.04880000	-1.00974900
C	-1.78538700	-0.72464300	-2.25307600
C	-0.50582800	-1.54672500	-1.94308500
C	-0.91254600	-2.87205300	-1.24080600
H	-1.44440300	-3.53144900	-1.94031100
H	-0.02026600	-3.39866400	-0.88344500
H	-1.57028500	-2.72224700	-0.38193700
C	0.12233600	-1.95809400	-3.29251300
H	0.98914100	-2.61160400	-3.13948400
H	-0.60759600	-2.51258100	-3.89497400
H	0.45077100	-1.09251700	-3.87227500
N	0.49966700	-0.76378100	-1.17572900
Li	2.41167100	-1.36149100	-1.32399100
O	3.16402800	-3.09318200	-2.02727200
C	2.82236200	-4.47018700	-1.74235300
H	1.74643500	-4.60510100	-1.90375100
H	3.04731200	-4.66581200	-0.68959100
C	3.65002100	-5.31058300	-2.71674800
H	4.64504700	-5.51215100	-2.30292600
H	3.17560100	-6.26971100	-2.94380400
C	3.75235700	-4.37833200	-3.93448300
H	4.59397300	-4.61489500	-4.59195800
H	2.83218500	-4.42272600	-4.52800600
C	3.89805600	-3.00555700	-3.27647000
H	4.94368100	-2.77139800	-3.04645800
H	3.47357700	-2.18549200	-3.86234600
N	4.06993700	-0.29927000	-0.84156100
C	5.21179100	-0.49197200	0.08202500
C	5.96682000	0.86021100	-0.03725500
O	5.38353800	1.49795900	-1.18941200
C	4.26271900	0.79026800	-1.50804000
C	3.41748500	1.34233400	-2.57877900
C	2.10993000	0.83042600	-2.79153600
C	1.40093000	1.44422800	-3.83961300
C	1.92775300	2.46405800	-4.63607000
C	3.22101000	2.93574300	-4.39742100
C	3.96369600	2.38007100	-3.36204900
H	4.96685400	2.74198700	-3.15797500
H	3.64240800	3.73193400	-5.00583500
H	1.33132100	2.89893100	-5.43654500
H	0.37737100	1.12318500	-4.03904100
H	7.04116400	0.75392000	-0.21127100
H	5.80596200	1.51157600	0.82978000
C	6.07497900	-1.66390400	-0.41588400
H	6.92246400	-1.83704200	0.25864000
H	5.47782900	-2.57954800	-0.46718500
H	6.46997800	-1.45469200	-1.41650200
C	4.72284900	-0.75587200	1.51089300
H	4.14089200	-1.68315300	1.55551900
H	5.57167800	-0.85693600	2.19833900
H	4.08729400	0.06158600	1.86526000
H	-2.53570300	-1.37090800	-2.73056500
H	-1.52883700	0.05431300	-2.98534900
H	-2.76052800	-0.80173000	-0.31317200
H	-3.22418700	0.58040100	-1.28783900
H	-1.68327300	1.26289900	0.58396000
H	-1.01602300	1.61962400	-1.00933200
C	-0.23815900	-0.89105100	1.24831600

H	0.63784300	-1.52642600	1.42685700
H	-0.39363800	-0.26951700	2.14038200
H	-1.10882800	-1.54435900	1.15774300
C	1.07628100	1.02632300	0.40954900
H	0.72992700	1.61082000	1.27071900
H	2.00831100	0.52687300	0.69439400
H	1.30089300	1.72127300	-0.40404800
H	1.23767500	0.02455200	-1.96604100





4-AS (N-bound)
G = –1204.980404
G_{MP2} = –753577.231

Atom	X	Y	Z
C	0.00000000	0.00000000	0.00000000
C	-1.11082700	-1.02996100	-0.33894500
C	-1.51290200	-1.88041200	0.86994100
C	-0.27520900	-2.53942600	1.48558600
C	0.83934500	-1.51932300	1.84449700
C	0.45206900	-0.74685200	3.13379300
H	1.17778100	0.05328000	3.32307200
H	-0.53979000	-0.29237900	3.08811600
H	0.45671500	-1.42250700	3.99941900
C	2.10733200	-2.32389200	2.19905600
H	2.91376400	-1.65886600	2.53089100
H	1.89345900	-3.01997200	3.01890500
H	2.47145800	-2.90438300	1.34738600
N	1.15251900	-0.63238200	0.69441100
Li	2.90225700	0.22244800	0.36523700
O	3.49779400	2.06661000	-0.02567700
C	4.34213700	2.28168900	-1.18730700
H	3.81609000	1.89951600	-2.07048500
H	5.26140000	1.70635900	-1.04970300
C	4.55945900	3.79401300	-1.26445400
H	5.42287800	4.09107000	-0.65768800
H	4.73132200	4.13548100	-2.28914900
C	3.25969800	4.33949000	-0.65162300
H	3.35317100	5.36198200	-0.27455800
H	2.45009300	4.31939600	-1.39009500
C	2.98616300	3.33024600	0.46313200
H	3.52045700	3.59062200	1.38603300
H	1.92575300	3.20030300	0.69263500
O	4.62822700	-0.55645600	0.82371000
C	5.55568300	-0.27613600	1.89639500
C	6.80238600	-1.13969600	1.54819700
N	6.30812200	-2.03904700	0.49083200
C	5.14622100	-1.65710200	0.13108000
C	4.30257000	-2.20705900	-0.94175600
C	2.93057700	-1.86466500	-1.06601800
C	2.26184400	-2.49476800	-2.13388700
C	2.88016800	-3.37733700	-3.02046500
C	4.23646800	-3.68136000	-2.86692000
C	4.94596700	-3.09773000	-1.82628700
H	5.99944400	-3.31778100	-1.67982700
H	4.73187900	-4.36686900	-3.54989500
H	2.30933200	-3.83397900	-3.82722800
H	1.19764100	-2.30129500	-2.27352100
C	7.94652000	-0.28648600	0.97442300
H	8.35890700	0.38396500	1.73870200
H	8.75031900	-0.93216300	0.60778200
H	7.59389600	0.32194200	0.13328500
C	7.28813000	-1.95916600	2.74966300
H	8.12141800	-2.60426600	2.45421200
H	7.62934500	-1.30411000	3.56090500
H	6.48522800	-2.59769800	3.13243500
H	5.74604500	0.80018600	1.90809600
H	5.08563300	-0.57483500	2.84008900
H	-0.55301500	-3.11877600	2.37742900
H	0.13807100	-3.25416100	0.75979700
H	-2.02861000	-1.26239400	1.61741700
H	-2.23586600	-2.64845800	0.56440300
H	-1.98703400	-0.51228000	-0.75458700

H	-0.73590900	-1.69853200	-1.12669500
C	-0.62542000	1.18162200	0.79266400
H	-1.26875000	1.78499000	0.13816500
H	-1.24016200	0.86088800	1.63586400
H	0.16464800	1.82953000	1.18981100
C	0.51066700	0.60721500	-1.32610500
H	-0.32351100	1.04250200	-1.88941300
H	1.23300700	1.41333900	-1.14008700
H	0.99340400	-0.13877600	-1.96159300
H	1.97086100	-1.27181700	-0.16422700

Chapter 2 References and Footnotes

1. Murakami, K.; Yamada, S.; Kaneda, T.; Itami, K. *Chem. Rev.* **2017**, *117*, 9302.

2. (a) Sartori, G.; Maggi, R. *Chem. Rev.* **2011**, *111*, PR181. (b) Smith, K.; El-Hiti, G. A. *Green Chem.* **2011**, *13*, 1579.

3. (a) Yang, Y.; Lan, J.; You, J. *Chem. Rev.* **2017**, *117*, 8787. (b) Shang, R.; Ilies, L.; Nakamura, E. *Chem. Rev.* **2017**, *117*, 9086. (c) Yang, L.; Huang, H. *Chem. Rev.* **2015**, *115*, 3468.

4. (a) Mongin, F.; Quéguiner, G. *Tetrahedron* **2001**, *57*, 5897. (b) Mongin, F.; Quéguiner, G. *Tetrahedron* **2001**, *57*, 4059. (c) Clayden, J. In *The Chemistry of Organolithium Compounds*; Rappoport, Z.; Marek, I., Eds.; Wiley: New York, 2004; Vol. 1, p 495. (d) Caubere, P. *Chem. Rev.* **1993**, *93*, 2317. (e) Schlosser, M.; Mongin, F. *Chem. Soc. Rev.* **2007**, *36*, 1161. (f) Hartung, C. G.; Snieckus, V. In *Modern Arene Chemistry*; Astruc, D. (Ed.), Wiley-VCH: Weinheim, 2002; Chapter 10. (g) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

5. (a) Bakker, W. I. I.; Wong, P. L.; Snieckus, V. *Lithium Diisopropylamide.* In *e-EROS Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley: New York, 2001. (b) Eames, J. Product Subclass 6: Lithium Amides. In *Science of Synthesis*; Snieckus, V., Ed.; Thieme; New York, 2006; Vol. 8a, p 173.

6. (a) Campbell, M.; Snieckus, V.; Baxter, E. W. In e-EROS *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley & Sons: Chichester; New York, 2008; Vol. 5. (b) Mulvey, R. E.; Robertson, S. D. *Angew. Chem., Int. Ed.* **2013**, *52*, 11470.

7. Fraser, R. R.; Mansour, T. S. *J. Org. Chem.* **1984**, *49*, 3442.

8. Owing to loose usage, we emphasize that driving force connotes exergonicity (thermodynamics).

9. (a) Cottet, F.; Schlosser, M. *Eur. J. Org. Chem.* **2004**, 3793. (b) Trecourt, F.; Mallet, M.; Marsais, F.; Quéguiner, G. *J. Org. Chem* **1988**, *53*, 1367. (c) Comins, D. L.; LaMunyon, D. H. *Tetrahedron Lett.* **1988**, *29*, 773. (d) Eaton, P. E.; Cunkle, G. T.; Marchioro, G.; Martin, R. M. *J. Am. Chem. Soc.* **1987**, *109*, 948. (e) Bridges. A. J.; Patt, W. C.; Stickney, T. M. *J. Org. Chem.* **1990**, *55*, 773. (f) Trécourt, F.; Marsais, F.; Güngör, T.; Quéguiner, G. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2409. (g) Gros, P. C.; Fort, Y. *Eur. J. Org. Chem.* **2009**, 4199. (h) Cottet, F.; Marull, M.; Lefebvre, O.; Schlosser, M. *Eur. J. Org. Chem.* **2003**, 1559. (i) Güngör, T.; Marsais, F.; Queguiner, G. *J. Organomet. Chem.* **1981**, *215*, 139. (j) Viciu, M. S.; Gupta, L.; Collum, D. B. *J. Am. Chem. Soc.* **2010**, *132*, 6361. (k) Hoepker, A. C.; Gupta, L.; Ma, Y.; Faggin, M. F.; Collum, D. B. *J. Am. Chem. Soc.* **2011**, *133*, 7135. (l) Fukuda, T.; Ohta, T.; Sudo, E.; Iwao, M. *Org. Lett.* **2010**, *12*, 2734.

10. (a) Groenendaal, L.; Van Loo, M. E.; Vekemans, J. A. J. M.; Meijer, E. W. *Synth. Commun*. **1995**, *25*, 1589. (b) Plé, N.; Turck, A.; Martin, P.; Barbey, S.; Quéguiner, G. *Tetrahedron Lett.* **1993**, *34*, 1605.

11. For discussions of possible slow regiochemical equilibration during an LiTMP-mediated orthometalation, see: (a) Mongin, F.; Desponds, O.; Schlosser, M. *Tetrahedron Lett.* **1996**, *37*, 2767. (b) Schlosser, M.; Marull, M. *Eur. J. Org. Chem.* **2003**, *8*, 1569. (c) Also, see reference 9l

12. Cantatore, G.; Cassandrini, P. Process for Preparing 2,2,6,6-Tetramethyl-4-Piperdone. U.S. Patent 4,536,581, August 20, 1985.

13. Previous orthometalations of substrates **1**–**4**: (a) **1**: Capel, V. L.; Dillon, K. B.; Goeta, A. E.; Howard, J. A. K.; Monks, P. K.; Probert, M. R.; Shepherda, H. J.; Zorina, N. V. *Dalton Trans.* **2011**, *40*, 1808. (b) **2**: Wang, L.; Wang, Y.; Guo, F.; Zheng, Y.; Bhadury, P. S.; Sun, Z. *Tetrahedron Lett.* **2013**, *54*, 6053. (c) **3**: Chadwick, S. T.; Rennels, R. A.; Rutherford, J. L.; Collum, D. B. *J. Am. Chem. Soc.* **2000**, *122*, 8640. (d) **4**: Bellamy, E.; Bayh, O.; Hoarau, C.; Tre´court, F.; Que´guiner, G.; Marsais, F. *Chem. Commun.* **2010**, *46*, 7043.

14. Wiedemann, S. H.; Ramírez, A.; Collum, D. B. *J. Am. Chem. Soc.* **2003**, *125*, 15893.

15. Computations and crystal structures of various MTMP derivatives: Armstrong, D. R.; Graham, D. V.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T. *Chemistry* **2008**, *14*, 8025.

16. (a) Hall, P. L.; Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. *J. Am. Chem. Soc.* **1991**, *113*, 9575. (b) Renaud, P.; Fox, M. A. *J. Am. Chem. Soc.* **1988**, *110*, 5702.

17. Romesberg, F. E.; Collum, D. B. *J. Am. Chem. Soc.* **1992**, *114*, 2112.

18. (a) Pratt, L. M.; Newman, A.; Cyr, J. S.; Johnson, H.; Miles, B.; Lattier, A.; Austin, E.; Henderson, S.; Hershey, B.; Lin, M.; Balamraju, Y.; Sammonds, L.; Cheramie, J.; Karnes, J.; Hymel, E.; Woodford, B.; Carter, C. *J. Org. Chem.* **2003**, *68*, 6387. (b) Balamraju, Y.; Sharp, C. D.; Gammill, W.; Manuel, N.; Pratt, L. M. *Tetrahedron* **1998**, *54*, 7357.

19. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.;

Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Gill, A.; Nanayakkara, C.; Gonzalez, M.; Challacombe, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian 09, Revision A.02; Gaussian, Inc.: Wallingford, CT, 2009.

20. (a) Collum, D. B.; McNeil, A. J.; Ramírez, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3002. (b) Algera, R. F.; Gupta, L.; Hoepker, A. C.; Liang, J.; Ma, Y.; Singh, K. J.; Collum, D. B. *J. Org. Chem.* **2017**, *82*, 4513.

21. We define the idealized rate law as that obtained by rounding the observed reaction orders to the nearest rational order.

22. Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. *J. Am. Chem. Soc.* **1991**, *113*, 5751.

23. (a) For attempted compilation of a comprehensive bibliography of triple ions of lithium salts, see: Ma, Y.; Ramírez, A.; Singh, K. J.; Keresztes, I.; Collum, D. B. *J. Am. Chem. Soc.* **2006**, *128*, 15399. (b) Also, see: Reich, H. J. *Chem. Rev.* **2013**, *113*, 7130.

24. One cannot rigorously exclude a combination of $[A_2S_3(ArH)]^{‡}$ and $[AS_3(ArH)]^{‡}$, but both suffer from steric demands associated with the high per-lithium solvation number.

25. (a) Liang, J.; Hoepker, A. C.; Bruneau, A. M.; Ma, Y.; Gupta, L.; Collum, D. B. *J. Org. Chem.* **2014**, *79*, 11885. (b) Liang, J.; Hoepker, A. C.; Algera, R. F.; Ma, Y.; Collum, D. B. *J. Am. Chem. Soc.* **2015**, *137*, 6292.

26. Algera, R. F.; Ma, Y.; Collum, D. B. *J. Am. Chem. Soc.* **2017**, *139*, 15197.

27. Gupta, L.; Hoepker, A. C.; Singh, K. J.; Collum, D. B. *J. Org. Chem.* **2009**, *74*, 2231.

28. (a) Sammakia, T.; Latham, H. A. *J. Org. Chem.* **1996**, *61*, 1629. (b) Stol, M.; Snelders, D. J. M.; de Pater, J. J. M.; van Klink, G. P. M.; Kooijman, H.; Spek, A. L.; van Koten, F. *Organometallics* **2005**, *24*, 743. (c) Jayasuriya, K.; Alster, J.; Politzer, P. *J. Org. Chem.* **1988**, *53*, 677. (d) Chadwick, S. T.; Ramírez, A.; Gupta, L.; Collum, D. B. *J. Am. Chem. Soc.* **2007**, *129*, 2259.

29. Reyes-Rodríguez, G. J.; Algera, R. F.; Collum, D. B. *J. Am. Chem. Soc.* **2017**, *139*, 1233.

30. (a) Hsieh, H. L.; Quirk, R. P. *Anionic Polymerization: Principles and Practical Applications*; Marcel Dekker: New York, 1996. (b) *Ions and Ion Pairs in Organic Reactions*; Szwarc, M., Ed.; Wiley: New York, 1972; Vol. 1 and 2.

31. (a) Bartlett, P. D.; Goebel, C. V.; Weber, W. P. *J. Am. Chem. Soc.* **1969**, *91*, 7425. (b) Al-Aseer, M. A.; Smith, S. G. *J. Org. Chem.* **1984**, *49*, 2608 and references cited therein. (c) McGarrity, J. F.; Ogle, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 1810. (d) Jones, A. C.; Sanders, A. W.; Bevan, M. J.; Reich, H. J. *J. Am. Chem. Soc.* **2007**, *129*, 3492. (e) Jones, A. C.; Sanders, A. W.; Sikorski, W. H.; Jansen, K. L.; Reich, H. J. *J. Am. Chem. Soc.* **2008**, *130*, 6060.